THE

PRACTICAL MEDICINE SERIES

COMPRISING TEN VOLUMES ON THE YEAR'S PROGRESS IN MEDICINE AND SURGERY

UNDER THE GENERAL EDITORIAL CHARGE OF

GUSTAVUS P. HEAD, M. D.

PROFESSOR OF LARYNGOLOGY AND RHINOLOGY,
CHICAGO POST-GRADUATE MEDICAL SCHOOL

VOLUME IX

ANATOMY, PHYSIOLOGY, PATHOLOGY, DICTIONARY

EDITED BY

W. A. EVANS, M. S., M. D.
ADOLPH GEHRMANN, M. D.
WILLIAM HEALY, A. B., M. D.

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ANATOMY AND PATHOLOGY.

W. A. EVANS, M. S., M. D.

Professor of Pathology, College of Physicians and Surgeons, Chicago; Pathologist to Cook County Hospital and Columbus Medical Laboratory.

PHYSIOLOGY AND BACTERIOLOGY.

ADOLPH GEHRMANN, M. D.

Professor of Bacteriology, College of Physicians and Surgeons, Chicago; Bacteriologist to Columbus Medical Laboratory.

DICTIONARY OF NEW WORDS.

WILLIAM HEALY, A. B. (HARV.), M. D.

Instructor in Gynecology, Northwestern University Medical School.

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SECTION I.

ANATOMY.

The Circle of Willis. *An examination of 706 specimens.* E. Fawcett and J. V. Blackford.[1] In this series of examinations the circle was found complete in 673, or 96.1 per cent. It was incomplete in 27 cases, or 3.8 per cent. When incomplete, the fault was due to: (a) absence of one or both posterior communicating arteries; (b) absence of the anterior communicating artery. The right posterior communicating artery was absent 13 times, or 1.8 per cent. The left was absent 10 times, or 1.4 per cent. Both posterior communicating arteries were absent 3 times, 0.4 per cent.

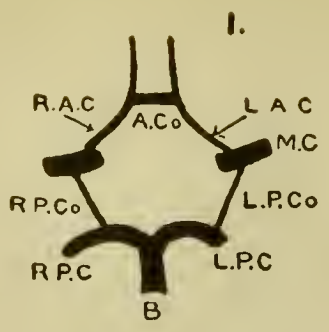
They noted absence of the anterior communicating artery only once.

The circle was symmetrical in 514 cases, 73.4 per cent. It was slightly more symmetrical in the male than in the female. It was complete and symmetrical in 510 cases, or 72.8 per cent. Here, too, the advantage was in favor of the male, the relation being as 76 to 66.7. The lack of symmetry was due to several defects. The right posterior communicating artery was larger than the left in 87 cases, 12.4 per cent. The left was the larger in 64, 9.1 per cent.

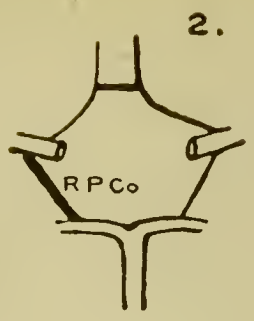
The right posterior communicating artery was absent 13 times, 1.8 per cent.; the left 10 times, 1.4 per cent. There was doubling of the anterior communicating artery twice.

The right posterior cerebral arose from the right internal carotid in six cases; the left posterior cerebral from the internal carotid in four cases. These last two causes

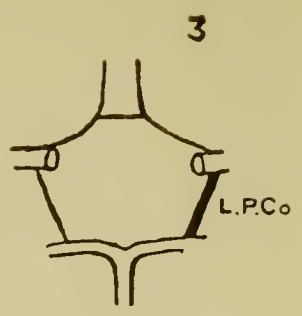
(1) Jour. of Anat. and Phys., 1906.



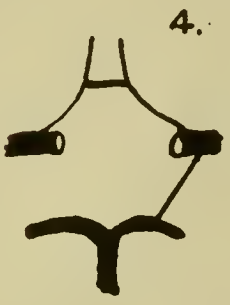
1. Complete and symmetrical, 72·8 per cent.



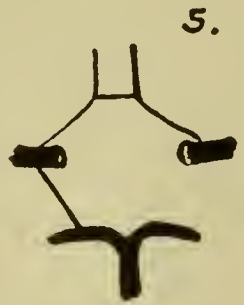
2. Right post. communicating larger than left, 12·4 per cent.



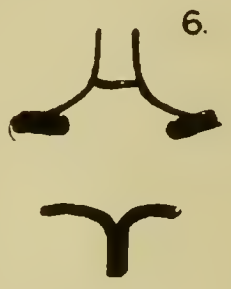
3. Left post. communicating larger than right, 9·1 per cent.



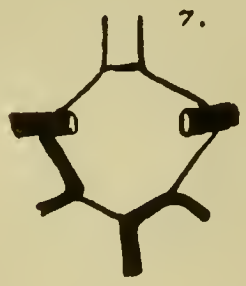
4. Right post. communicating absent, 1·8 per cent.



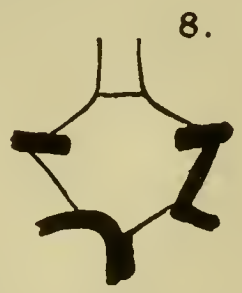
5. Left post. communicating absent, 1·4 per cent.



6. Both post. communicating arteries absent, ·4 per cent.

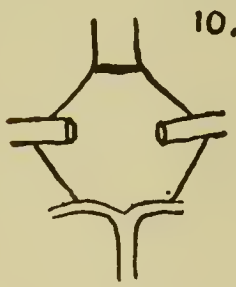


7. Right post. cereb. from int. carotid, ·85 per cent.

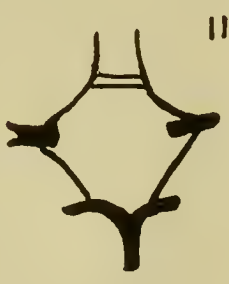


8. Left post. cereb. from int. carotid, ·57 per cent.

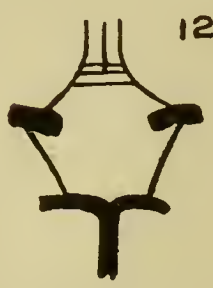
9. Both post. cerebrals from int. carotids, ·14 per cent.



10. Ant. communicating single, 92·1 per cent.



11. Ant. communicating double, 7·2 per cent.



12. Ant. communicating treble, ·14 per cent.

FIG. 1

B.—Basilar artery.
R.P.C.—Right post. cerebral artery.
L.P.C.—Left post. cerebral artery.
R.P.Co.—Right post. communicating.
L.P.Co.—Left post. communicating.
M.C.—Middle cerebral artery.
L.A.C.—Left anterior cerebral.
R.A.C.—Right anterior cerebral.
A.Co.—Anterior communicating.

of asymmetry were about twice as frequent in females as in males. The anterior communicating artery was absent once. It was single in 645 cases, 92.1 per cent. It was double in 51 cases, 7.2 per cent. It was treble in one case, in which there was also a third anterior cerebral artery. Twice the artery was H—shaped.

In 23 cases there was a third anterior cerebral artery, 3.2 per cent.; of these, nineteen were in males and four in females. The third artery arose, as a rule, from the anterior communicating; once it arose by two roots, one from each anterior cerebral. In two cases it arose directly from the left anterior cerebral.

In two cases the basilar artery, after giving off two posterior cerebrals, bifurcated into two posterior communicating arteries.

The Facial Expression of Violent Effort, Breathlessness and Fatigue. R. Tait McKenzie[1] made careful observations on the subject. In violent effort there is a general converging of the lines to the root of the nose, the transverse wrinkles at that point marking the action of the pyramidalis nasi. The frowning brows are drawn down and the palpebral fissure is narrowed to a mere slit. The outer angle of the eye shows the crow's-feet that accompany the strong action of the orbicularis palpebrarum. The sneering expression of the nose, caused by the action of the compressor nasi, is like the snarl of a dog, while the levator anguli oris exposes the canine tooth and increases the effect. The nostril is distended, the upper lip is raised from the teeth, and the direction of the naso labial fold is altered. The lower lip is drawn tightly across the clenched teeth, except at the corners of the mouth, where it is pulled away by the platysma, leaving little pouches at each angle. The general impression of the face is repulsive. Hatred, menace and rage predominate, with a feeling of distress about the strained mouth and neck.

When effort is prolonged to the point of breathlessness the facial expression becomes radically changed. The smoothness of the forehead is broken by wrinkles spreading out from the inner end of the updrawn eyebrows, drawn upward and inward by the corrugator supercilii, the

(1) Journal of Anatomy and Physiology, 1906, p. 511,

muscle of pain, grief, mental distress, and anxiety. The upper eyelids droop and half cover the eye. The nostrils are widely dilated, the mouth gapes, and the lips are retracted. The raised upper lip and the deepened and changed naso-labial fold add to the look of pain, while the down-drawn mouth angle, the tongue close pressed against the teeth, the cheek sunken into the cleft between the opened jaws, all go to increase the haggard look. The general pose of the head is backward, the chin thrust forward, and the neck convulsed by the sterno-mastoid, the platysma, and the other extraordinary muscles of respiration. In fatigue the eyebrows show a slight frown, and the eyelids are heavy, as with sleep. The upper lid is retracted irregularly from the teeth. The mouth is half open, and the lower lip hangs loosely from the parted teeth. The eyebrows have the appearance as though one were watching a distant object in an uncertain light. The general effect is one of vacancy.

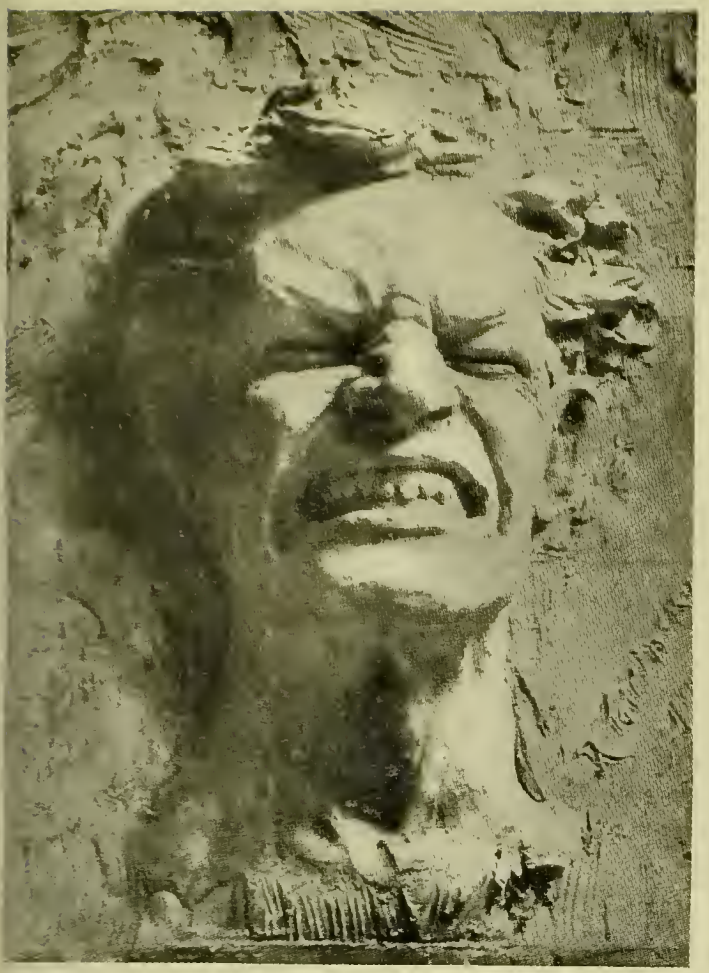
In advanced fatigue there are long, doubly curved wrinkles across the forehead, with arched eyebrows. The nostrils are dilated and the lips drawn outward and downward by the platysma. The head is thrown backward and the chin forward. This pose of the head is characteristic of extreme fatigue. See Plate I.

Anatomy of the Inguinal Region. There is no part of the body where the usual surgical procedures of the region require better knowledge of anatomy and physics than the inguinal region. Witherspoon[1] summarizes his study as follows: The internal abdominal opening is located in the extraperitoneal fatty tissue.

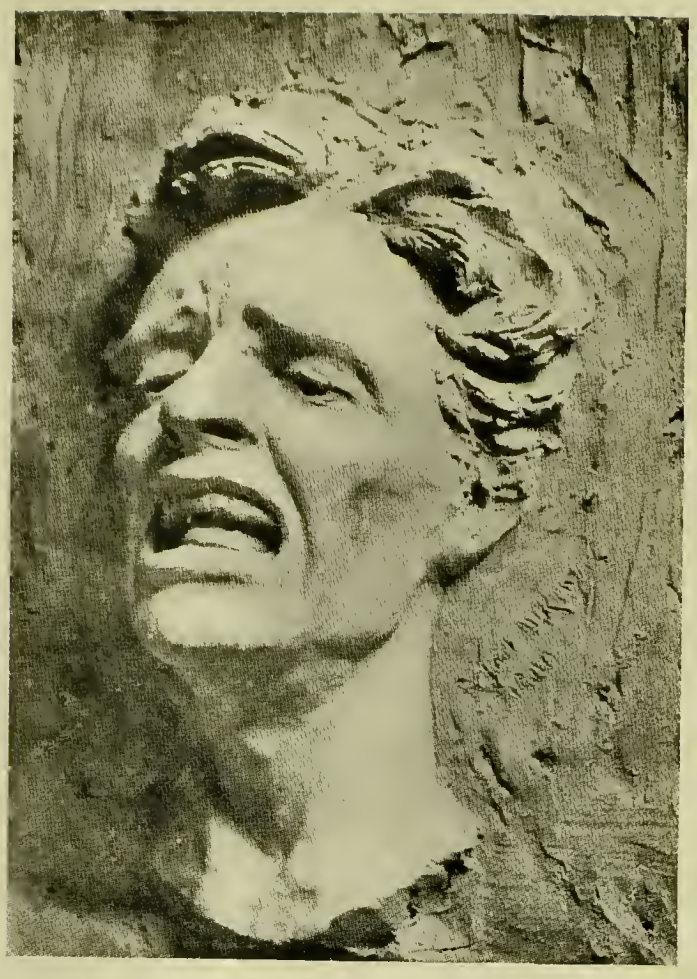
Hesselbach's ligament is formed by fibrous bundles which connect the outer end of the semi-lunar fold of Douglas with the inner margin of the internal abdominal opening. These bundles are developed chiefly in the extraperitoneal fatty tissue. Along the route of these bundles there exists between the fatty tissue and the transversalis fascia a close union. During intra-abdominal pressure, Hesselbach's ligament, due to its resistance, helps to increase the size of the internal abdominal opening.

In the inguinal area the internal surface of the ab-

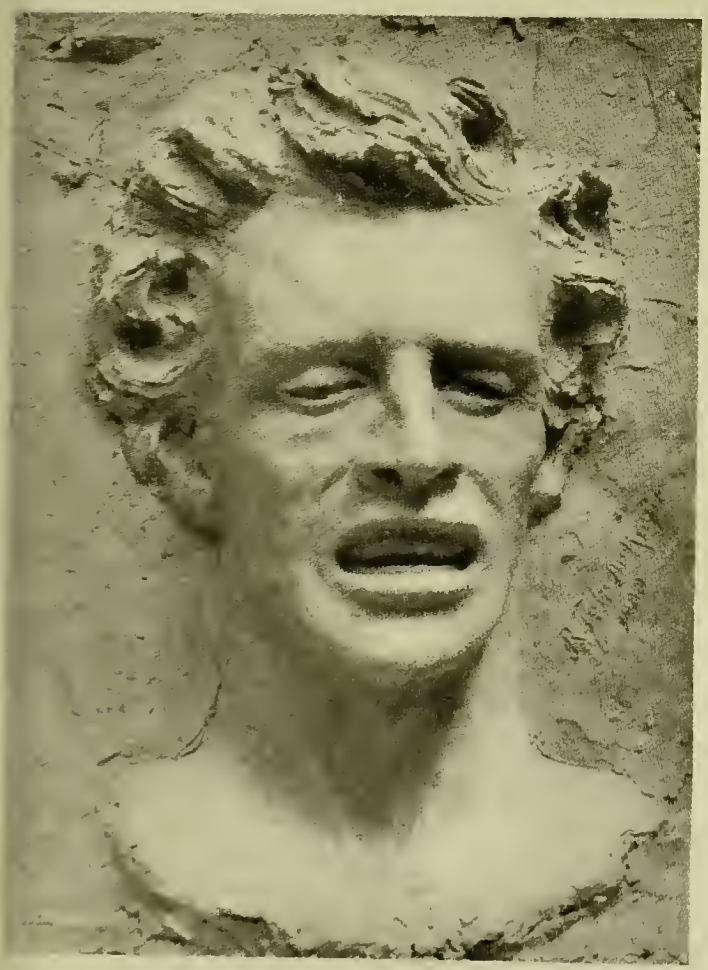
(1) Jour. Amer. Med. Assoc., May 19, 1906.



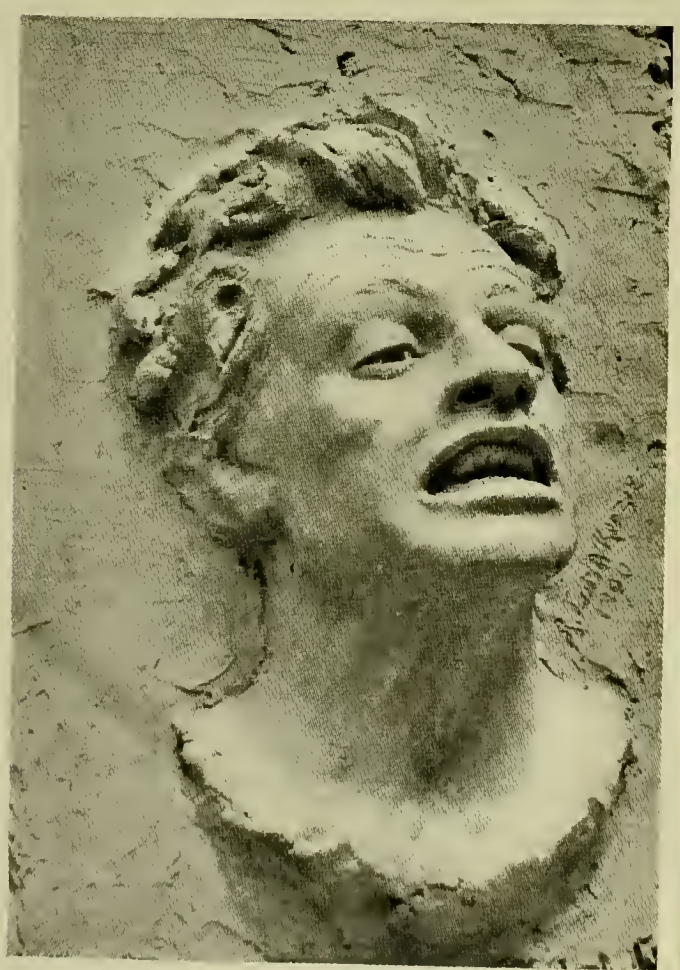
No. 1. Violent Effort.



No. 2. Breathlessness.



No. 3. Fatigue.



No. 4. Advanced Fatigue.

PLATE I.

dominal wall is divided into two planes by Hesselbach's ligament. Normally, the plane lateral to this ligament is only slightly anterior to the plane median to the ligament. When the muscles of the lateral plane are weakened by disease or are enfeebled through advanced age intra-abdominal tension greatly exaggerates this difference. As the internal abdominal opening is situated at the junction of these two planes, the greater the difference the more patulous the opening and the greater the possibility of escape of a viscus through the opening.

The transversalis fascia does not join Poupart's ligament at any point.

The deep crural arch is formed by the junction of the transversalis and cremasteric fascias in the arch in front of the external iliac vessels as they pass into the thigh. The free (posterior) edge of Gimbernat's ligament is just external to and parallel with the deep crural arch.

The fibrous bundles which pass out of the pelvis into the so-called conjoined tendon give to the abdominal wall its chief strength internal (posterior) to the inguinal canal. The aponeurosis of the transversalis muscle strengthens the wall just internal (posterior) to the external abdominal ring.

The base of the so-called conjoined tendon, the lateral margin of which is formed by the fibrous bundles which enter the tendon from out of the pelvis, is the constricting agent in femoral hernia. A Spanish surgeon, Gimbernat, attributed this agency to the structure which has since been given his name.

The so-called conjoined tendon was in no instance formed by a union of fibers from the internal oblique and transversalis muscles in the subjects dissected. Judging from the usual anatomic arrangement this union seems quite impossible.

The external abdominal opening is situated between the dividing fibers of the aponeurosis of the external oblique muscle. The external abdominal ring is situated in the periaponeurosis which covers the external abdominal opening.

Surgical Anatomy of the Prostate. Walker[1] found that

(1) Journal of Anat. and Phys., 1906. Proceedings, p. vii.

the sheath of the prostate is formed by the recto-vesical fascia and envelops the organ, except at its basal attachment to the bladder and at the apex where it becomes incorporated with the striped muscle surrounding the urethra. The sheath may be stripped off the prostate in the lateral and posterior surfaces, but not along the anterior surface, where it is firmly adherent to the organ. The anterior portion of the sheath differs from the rest of the envelope. It is firmly adherent to the prostate, and is not formed by the layer of fascia which passes down over the lateral aspects of the gland. In the surface of this part of the sheath is a thin layer of fascia, which corresponds to the upward reflection of fascia over the bladder. Beneath this is a thick band, the fibers of which are irregularly set, and imbedded in them are masses of fat and non-striped muscle and the veins of the prostatic plexus.

The prostate is adherent to the under surface of the bladder base and extends backward for about one-half inch behind the urethra to about the middle of the trigone. The greatest lateral extent is in a line passing outwards and backwards from the urethra, and measures about 9/16 of an inch on each side. The trigone of the bladder is a definite muscular triangle which is formed by a band of muscle passing between the ureters and a band from each ureter to the urethra. These bands unite and pass on into the wall of the urethra.

Beneath these longitudinal fibers is a flat layer of circular fibers, which may be distinguished from the rest of the circular bladder muscle. This layer becomes thicker as it approaches the urethra, and forms a wedge behind the urethral opening, and then passes on into the urethral wall. The circular muscle is not found in the bladder wall in front of the urethra, but forms a thick layer along the anterial wall of the prostatic urethra. The non-striped sphincter is formed by these layers of circular muscle. The outer longitudinal layer of bladder muscle is inserted into the base of the prostate.

The ready stripping of the sheath of the prostate is an important point in the operations of perineal and supra-pubic prostatectomy. For the supra-pubic operation certain changes are necessary in the bladder base.

The sphincter is dilated by the protrusion of a nodule of prostate into the bladder, and the finger can thus be pushed through the lumen of the sphincter, and need not penetrate through the muscle of the bladder floor.

The striped muscle in relation to the prostate forms a ring surrounding the urethra at the apex of the gland. Thence it passes up beneath the anterior layer of the sheath as far as the bladder wall. This striped muscle probably plays an important role in retaining the urine after supra-pubic prostatectomy.

The prostatic plexus passes up the front of the prostate, and at the junction of this organ with the bladder gives off two branches which surround the bladder neck at its junction with the prostate. The shape of the whole plexus is roughly that of the letter Y.

The principal veins of the plexus lie imbedded in the thick band of fascia which forms the anterior layer of the sheath, and do not come into direct relation with the capsule of the gland.

The prostatic urethra is vertical and straight at its supra-frontal part, but below the verumontanum it curves forward. The prostatic urethra is removed with the prostate in the majority of cases of supra-pubic prostatectomy without causing any change in the sensory part of the reflex act of micturition.

The gland tissue of the prostate is in the form of a horseshoe at the base of the gland, with the urethra in the same plane as the anterior border of the lateral lobes. No separate middle lobe could be found. The capsule of the organ was the unappropriated margin of the non-striped muscle stroma.

The seminal vesicles were placed horizontally along the upper borders of the prostatic lobes.

Anatomy of the Duodenum. Ochsner[1] reports further observations on what might be termed a duodenal pylorus or sphincter. It is composed of a localized thickening of the circular muscle fibers of the duodenum. This thickening is usually situated 3 to 10 cm. below the ampulla of Vater. It may be located just at that orifice. The band is usually single, though it may be double with an inter-

(1) Amer. Jour. Med. Sc., July, 1906.

vening area of muscle of normal thickness. The presence of this sphincter is responsible, in the opinion of Ochsner, for the frequency of duodenal ulcer, of vomiting of bile, and of dilatation of the stomach in chronic irritations further down the tract, *e. g.*, chronic appendicitis.

SECTION II.

PHYSIOLOGY.

Regeneration. Morgan[1] discusses the extent and the limits of the power of regeneration in man and other vertebrates. Regeneration is only one phase of the general phenomenon of growth. Why is it, then, that an animal that has ceased to grow begins to regenerate with great rapidity when a part is removed? On the other hand, why does an animal stop growing? It would not seem that an animal stops growing because its cells have lost their power of further growth. In a cut surface new growth at once commences, and not entirely by reserve cells but from the formed tissues of the older part. The cells in all parts of the body with few exceptions possess this power for further growth. In fact, cells seem to have limitless power in this direction and something in the body must restrain their activity after a certain size has been reached.

It is sometimes assumed that the balance of food absorption leads to a stage of equilibrium. If this is a fact the removal of a part should lead to increased weight by growth in the rest of the animal, because more food is now available for its nutrition. If the tail of a salamander is cut off one would expect that the animal's weight would increase rapidly to the amount of weight removed in the tail and that as the new tail grew it would remain constant, the general body losing as the tail grew from day to day. Following is a table showing such changes in weight.

(1) Jour. Amer. Med. Assoc., May 5, 1906.

Table showing gain in weight in *Dimyctylus* with tails cut off at base and tails not cut off:

Without tails.	Date.	Check animal.
1.23	Dec. 12	1.85
1.28	Dec. 13	
1.49	Dec. 18	1.70
1.53	Dec. 27	1.66
1.83	Jan. 5	1.98
1.90	Jan. 13	2.06
1.91	Jan. 20	2.13
2.07	Jan. 27	2.37
2.02	Feb. 3	2.19
2.13	Feb. 10	2.23

As is shown the tailless animal increased rapidly at first and in a week had made good the loss from the removal of the tail. It was found that the increase in weight is not due to a storing up of fat but is due to an increase in all the organs and parts of the body. Is this condition due to the amount of food available? If two sets of animals without tails are compared, one set being starved and one set being fed, it will be found that the tails in both grow at about the same rate. It will now be found that the starved animals have become greatly emaciated, but that their tails have been growing at nearly a normal rate. The regenerative power is not determined by the amount of food, but it would seem to be due rather to the greater assimilative power of the cells of the new part. Another curious fact is that seen in similar experiments upon other animals, especially crayfish. If more legs are removed the new legs grow faster in proportion to the larger number to be replaced. It has been proposed to explain this by the fact that if more legs are removed there is at once more food available for regeneration. The writer tested this point as in the preceding by starving one set and not another and found that very little difference was to be noted. He concludes, therefore, that food supply will not explain the results.

The rate of regeneration is also different; if the tails of fishes are cut off near the base regeneration takes place faster than when only the tip is cut away. In fact, the

entire tail may regenerate in about the time that it would be necessary for one-half in another fish. The same is true of the arms of starfish and the posterior ends of earth worms. An explanation is hard to find. It would seem, however, that the influence that determines the rate of growth of the removed part is similar to that influencing the growth of the entire animal. The young animal grows faster and then more and more slowly as maturity is reached.

The writer advances the view that as cells generally have unlimited power of growth some inhibitory force is of more importance than a stimulative influence in the determination of the rate of growth. This may be a condition of pressure upon the cells. Thus the size of an adult animal is determined by the differentiation of its cells and the differentiation is regulated by the mutual pressure of the cells on each other. Among vertebrates regeneration can be seen in fish, salamanders, tadpoles. Lizards can regenerate the tail but not the legs. The new tail, however, is imperfect. In birds the beak alone is the only external part having the power to be replaced when broken off. Finally, in mammals neither the limbs, tail or other external parts have power to regenerate if they are removed.

The writer offers as an explanation for the failure of regeneration in man, the fact of the highly specialized character of the cells and the great variation in their rate of regeneration leading to an entire failure in co-ordination. The different structures as skin, muscle, bone and nerve, all regenerate individually. The bones probably give most difficulty because of their slow growth. If a modification of activity could be induced it might be possible to induce a co-ordination between structures that would greatly increase the regenerative power in the higher vertebrates and in man.

Protein Nomenclature. Halliburton,[1] in his introductory remarks at the opening of the Section of Physiology of the British Medical Association, selected this subject for consideration. This matter has been passed upon by a joint committee of the Physiological and Chemical Socie-

(1) Brit. Med. Jour., Sept. 8, 1906.

ties of England. After much debate the word "protein" was recommended as the general name for this class of substances. It is at present so used in America, England and to some extent in Germany (Proteinstoffe). The word "proteid" should no longer be used.

The arrangement of the subclasses beginning with the simplest would be as follows:

1. Protamines.
2. Histones.
3. Albumins.
4. Globulins.
5. Sclero-proteins.
6. Phospho-proteins.
7. Conjugate proteins.
    a. Gluco-proteins (Miecin).
    b. Nucleo-proteins.
    c. Chromo-proteins (Hemoglobin).

The term conjugate protein is retained because of the inability to find a single word to express the qualities of this subclass, and further because it implies that the protein molecule is combined with a prosthetic group. The vitellin-caseinogen group is now passed with the phospho-proteins. The prefix nucleo, often used in connection with these substances, is considered as being incorrect. The new word sclero-protein replaces the word albuminoid (gelatin, keratin, etc.). The prefix indicates the skeletol origin and the often insoluble nature of its members.

The terms recommended for the products of protein hydrolysis (not proteolysis) are as follows:

1. Infra-protein.
2. Proteoses.
3. Peptones.
4. Polypeptides.

Infra-protein replaces albuminate (acid albumin, alkali albumin). The termination *ate* implies a salt and on this account is objectionable. The term "proteoses" includes albuminose, globulose, gelatose, etc.

The household word "peptone" is not likely to disappear from literature. It is proposed, however, that it be restricted to those further products of hydrolysis, which cannot be salted out from solutions but which nevertheless give the biuret reaction. The polypeptides are still further

on the down grade, though most of them are synthetical products of amido-acids. They do not as a rule give the biuret reaction.

In regard to the muscle proteins the terms "paramyosinogen" and "myosinogen" are to be retained for the proteins of the muscle plasma and soluble myosin and myosin for the final products.

Amido-acids and Metabolism. Barber's[1] article is a detailed consideration of this subject. The problems of metabolism are the most interesting questions of internal medicine today. Bacteriology and parasitology have, until recently, brought to us, as physicians, useful discoveries; lately, however, physics and chemistry are opening the way to a newer stage of progress. The organic chemists, with Emil Fischer at their head, have greatly assisted in this matter by clearing up the constitution and behavior of sugars and purins. Carbohydrate metabolism as a study has been much advanced by their ideas concerning glucose, fructose, xylose, and arabinose. In the same way ideas about purin nucleus, the pyrimidin ring and imidazol have made the problems of nuclein metabolism approachable. With these substances the proteins represent the acme of chemical complexity. Their complex structure, their highly inconvenient physical properties and the difficulty of obtaining them in a pure state has made their study very difficult. Recent active investigations have led to the discovery that in spite of the enormous complexity of the protein molecule they are, at least in one respect, more simple than could have at first been guessed—they all consist of long chains of relatively simple atom groups, into which they may be split by hydrolysis. Nearly all of these are what are known as the amido-acids. There are numbers of these amido-acids; how many is not known. In serum albumin there are at least a dozen varieties, because they have been isolated and rough quantitative estimations have been made. The albumins, globulins, albuminoids, albumoses, and peptones consist apparently of chain groupings of these amido-acids. Obviously these bodies must form the basis of the whole protein metabolism.

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(1) Brit. Med. Jour., Oct. 27, 1906.

The chemistry of the amido-acids has an important bearing on the protein constituents of our food stuffs. They have been isolated from various foods. Chemistry shows them to be composed of carbon, hydrogen, oxygen, nitrogen and sulphur. Physically they have a colloidal nature and further undergo a peculiar change known as denaturalization. Owing to these properties the physiological chemists have been able to separate several dozen different proteins. The most complex are the proteids or proteins proper, combined with other substances as nuclein, hematin, or glucosamin. The simpler proteins are divided into two groups: first, one made up of substances like the albumins, globulins, gliadin, myosin, and casein; and second, the so-called albuminoids, as collagin, heratin, elastin, reticulin. Some of these can be obtained in a crystalline condition, although their purity is doubtful. The action of acids and alkalies upon their bodies has been studied.

Concerning the nature of some of the resulting products something is known concerning leucin and tyrosin, but about most of them there was no knowledge until recently. New methods of separating the amido-acids have been devised and their chemical relations established further, so that it has been possible to unite them into shorter or longer chains, producing amido-like aldydrides, or the so-called peptides and polypeptides. Some of these possess external properties as color reactions and behavior to acids and alkalies similar to peptones, so that they may be considered as near relatives and the beginning of a synthesis of these bodies. Following are some of the amido-acids that have been obtained by hydrolytic cleavage: Glycocoll, alanin, amido-valerianic acid, leucin, isoleucin, protin, serin, phenylanin, glutaminic acid, aspartic acid, tyrosin, cystin, tryptophan, lysin, histidin and arginin. Nearly all these amido-acids have been made synthetically and they have been combined as acyl and phenyl compounds and as amides and acid chlorids. The esters are strong bases: it is upon the formation of esters and their subsequent separation by fractional distillation that Fischer's ester method of separation depends.

All of the amido-acids from proteins except glycocoll contain asymetrical carbon atoms and consequently are optically active. It has been found by the work of several

investigators that the same amido-acids are present in most foods, but in considerably different amounts. Exceptions may be noted in that egg albumin contains no glycocoll, gliadin from wheat contains no lysin and glatin and is devoid of tyrosin and tryptophan.

The variety of forms possible is almost infinite because of the wealth of combination possibilities and because of the large numbers of isomers that may exist because of asymetrical carbon atoms. There may also be different rings, as piperazin and the ester and ether groupings. Nature has here attained her highest chemical performance and has far outstripped the carbohydrates and fats in the wealth of chemical forms.

In the alimentary tract the digestion and assimilation of the proteins has in its first action an hydrolysis by the ferments, pepsin and trypsin. The use of pure gastric and pancreatic juices in these experiments has much improved the accuracy of the findings. The hydrolytic action proceeds by stages. The gastric juice swells up proteid food, splits off glucose, nuclein and hematin from the nucleoproteids and attacks the proteins themselves, breaking the huge molecules into albumoses and peptones. The cleavage goes on still further because bodies that do not give the biuret reaction are formed, but it stops short of the production of amido-acids. The pancreatic juice also splits by hydrolysis but goes much further. Free amido-acids begin to appear early in this digestion. Tyrosin is one of the early products. There are, however, protein groups that resist tryptic digestion and can be further split or hydrolyzed after digestion is finished. The whole series is present in tryptic digestion, but there still remain quantities of material to which the name polypeptide has been given. These are as yet very incompletely understood. HCl alone can split them all.

What is the meaning of the far reaching disintegration of the protein molecules as it occurs during digestion? It might seem that the protein molecule would be absorbed as such and used directly in tissue metabolism. Such is not the case. Every animal species and possibly individuals have their own specific proteins. The injection of serum albumin and albuminous extracts leads to the formation of specific pricipitins. The serum albumin of each

animal maintains an extreme constancy of composition, no matter what kind of protein is fed. The process of digestion, ferment action, not alone break down the foreign proteins to make them absorbable but further to make it possible that the body may synthetize its own proteins from the fragments. As the proof of the presence of these different bodies in the blood is yet unsettled and offers many difficulties no definite statements can be made, but it would seem that the intestinal wall is highly selective in its power towards the products of digestion and probably synthetizes to a certain extent from broken down protein contents in the intestine. The individual tissue cells are therefore quite independent, as it is the function of the intestine to supply them with the specific proteins they desire in a continuous manner. The importance of the intestine to the functions of the body is therefore more important than ever.

The relation of the cell to the serum portions next deserves attention. There is much evidence of a local tissue hydrolysis. The cells have the same classes of material presented, their work is simplified, but there is more to be done before the specific proteins of the organs are evolved. The enzymes of the cells cause further disintegration, while by synthesis the peculiar amido-acid complexes of the cells are produced. Unused cell groups are rejected, to be used elsewhere, and the more or less speedy combustion of the carbon chains goes on simultaneously with the other changes. The exact nature of these changes is not well known. There is in all probability a constant flux of cell proteins. This is necessary because there are undoubted evidences of constant replacement. Constant repair must be accomplished by active measures and the cells must stand ready to reproduce their kind whenever necessary. In dead tissues, where cell ferments are left uninjured, protolysis or autolysis occurs and gives rise to amido-acids in abundance. Amido-acids do not appear in the urine except under unusual conditions. Ferments may split the amido-group with formation of ammonia and this in turn unites with carbonic acid and an amido-residue forming urea. In cystin urea the patient cannot disintegrate the cystin formed in the cells. Perhaps the necessary ferment is absent. It also happens that some of

the amido-acids are caught before complete disintegration and are combined with other chemical substances. Thus normally a certain amount of glycocoll is continually being caught by benzoic acid and being synthetized in the kidneys into hippuric acid. This catching of amido-acids may lead to an important method of experimentation and in a practical way is of service in rendering poisons innocuous.

The formation of sugars from albumin has been much discussed. It is now known that the liver can split leucin with the formation of acetone. The long non-nitrogenous chains set free in such process may also have to do with the synthesis of glycerin, fatty acids and fat. There is, therefore, more simply a destruction in all these changes.

Proteolytic Ferments. The interesting question concerning the identity of the proteolytic ferment and milk coagulating principles in the gastric and pancreatic juices is discussed by Hemmeter.[1] Pawlow and Parastschuk are the strongest supporters of the affirmative in this question. The generally accepted opinion among physiologists has been that the gastric as well as the pancreatic secretions contain two distinct enzymes for these activities. The properties ascribed to chymozin probably belong to pepsin. In the case of the human gastric secretion milk is coagulated in the presence of a normal amount of HCl, but it does not curd when the juice is strictly neutralized. Pawlow found that a distinct proteolytic action could be obtained with filtrates of neutralized dog gastric juice (Hammarsten's method of separation) when diluted 5-10 times with dilute HCl solution, while ordinarily this filtrate only coagulates milk without digesting fibrin. In these observations the injurious effect of alkali was the main factor.

The two ferments may be separated by another method. When gastric juice is heated to 65° C. for ten minutes, chymozin is destroyed and only the proteolytic activity is preserved. By the Schrumph method a pepsin solution free from proteid can be prepared so that it shows proteolytic activity but no milk-curdling action at all. This method is one which entirely overcomes the objection that the loss of the milk-curdling action is due to foreign addi-

(1) Berlin. klin. Woch., Oct. 30, 1906.

tions. If pepsin and chymozin belong to the same molecule there should be a similarity in action and a certain proportion between the work of the two. On the other hand, when the two activities do show a close parallelism, it does not exactly discredit the theory that the effects of the two may be due to two different molecules. To subject a digestive secretion that gives evidence of two strikingly different effects to varying external influences, and thereby show that the effects increase or diminish together, or disappear together, can hardly be considered a sound form of experimental logic, and the claim that these effects are due to the same agent in the two remains unproven.

It may be that, in the course of practical examinations of stomach contents, some persons show an absence of free hydrochloric acid, but combined hydrochloric acid will be present whenever they give the biuret reaction with an Ewald test meal and show no coagulating activity.

The conclusion seems justified that pepsin is present in such cases, and chymozin absent; this, however, is difficult to harmonize with the view of Pawlow, that the proteolytic and the milk-curdling effects are due to the same molecule.

Autolysis Levene's[1] articles have as objects the elucidation of the nature of all chemical reactions that make the functions of the body possible; to interpret the role of the individual organs in animal metabolism; to study the intermediate products of metabolism.

Since there was some foundation for the view that the process of autolysis is the one which controls tissue disintegration, it seemed important to make clear whether or not the mechanism is capable of breaking down albuminous matter derived from other sources than that of its own body substance. The first observation in this direction was made by Theobald Smith, who noted that fresh tissues removed from the organism under aseptic conditions were capable of digesting gelatin. On the other hand, Martin Jacoby noted that during the process of liver autolysis, of the proteids, only the globulins suffered a disintegration; and in a later work he observed that the self-digesting liver was completely incapable of digesting lung tissue. Thus, on the basis of this work,

(1) Jour. Amer. Med. Assoc., March 17, 1906.

one would be led to the view that the process of autolysis is incapable of causing the digestion of circulating proteid, and that the two processes are totally independent one of another. However, Hedin has shown that the spleen possesses the power to digest not only its own proteid material but also the proteids of the blood. Thus the question still remains an open one.

The work thus far reviewed possessed primarily theoretical interest only. It aimed to elucidate the mechanism controlling the disintegration of tissue components in the living and in the surviving organs. Nevertheless a detailed knowledge of the products of tissue autolysis is of importance from the standpoint of practical medicine. In the human organism, as well as in that of many animals, all substances which are consumed as food and nourishment, no matter how greatly they differ in their chemical composition, are finally broken down into a few very simple bodies which are rejected by the organism through the kidneys, bile and other excretory mechanisms. Urea and carbonic acid are the two substances into which nearly all foodstuff is transformed. In a complex organism the metamorphosis is a gradual process. Before a nitrogenous substance is transformed into urea it undergoes numerous degradations. Before sugar is oxidized to carbonic acid it suffers numerous changes. Further, it is not improbable that in a very complex organism individual organs are concerned only in one definite phase of the transformation, leaving the other organs to continue and to complete the work. In his recent address on this subject Professor v. Noorden pointed out that the information regarding the nature of intermediate products of metabolism, as well as the seat of their formation, is lacking. Attention of investigators has turned to the study of the products of autolysis of various organs in the hope of filling in the gap in our knowledge of the mechanism of nutrition and of self-preservation of the organism.

However, the study of the substances arising in the course of autolysis was preceded by very active work on the normal composition of tissues and tissue components. Indeed, it was to be expected that within the body tissue constituents would break down into their component parts. Recent years are marked by astonishing progress in the

knowledge of the chemical nature of tissues. It was owing to this progress that the study of autolysis was made a comparatively easy matter. As already stated, the principal tissue components are albuminous matter, sugars and fat. The changes which each one of these components undergoes in the course of self-digestion has been the subject of special investigations.

Under the term proteid is generally understood the substance which represents the most important and most characteristic part of living matter. It is colloidal in nature and is composed of various nitrogenous acids. On heating proteid with strong acids or alkalies, the original substance disappears, giving rise to the nitrogenous acids. Of those already known are the following:

Glycocoll.	Lysin.
Alanin.	Arginin.
Aminovalerianic acid.	Histidin.
Leucin.	Prolin.
Glutamic acid.	Tryptophan.
Phenylalanin.	Cystein.
Tyrosin.	

Of the proteids, one group attracts special attention. Its members are present in greatest quantity in the nuclei of all cells, and it has been assumed that the function of the nucleus is closely associated with the presence of these substances. They are named nucleins, nucleoproteids, nucleoalbumins, etc. They are more complex than ordinary proteids, containing in their molecule, besides the usual constituents, a body termed nucleic acid. This acid is composed of substances to which a considerable role in the pathogenesis of disease has been attributed. Its components are as follows: Phosphoric acid, carbohydrate, thymin, uracil, cytosin, adenin, guanin, hypoxanthin.

Normally, components of simple and complex proteids occur as such in tissues in very insignificant quantities. But it is found that in the course of self-digestion an organ may undergo such deep changes that nothing remains of its original structure, in its place the following substances appearing:

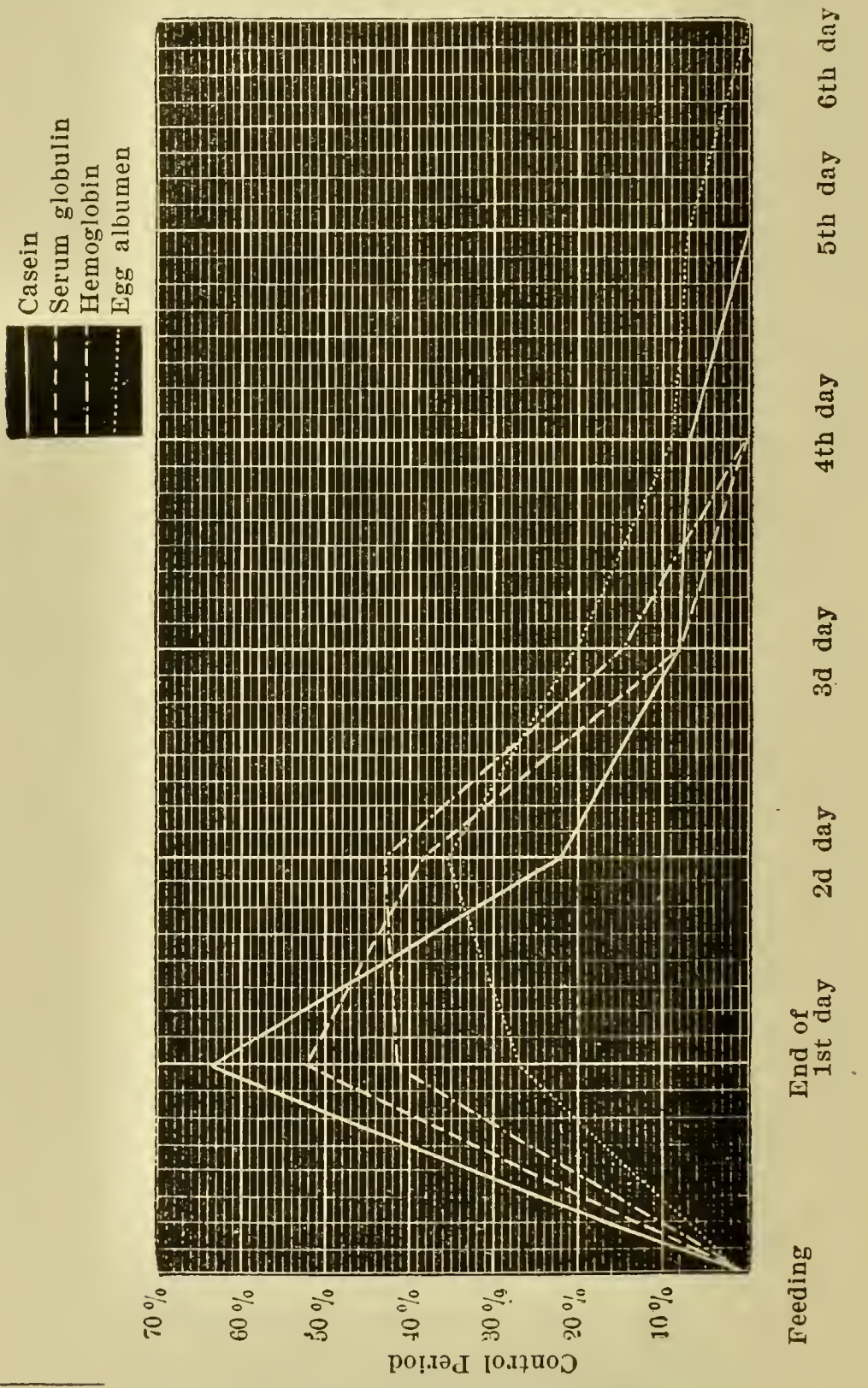
	Pancreas.	Liver.	Spleen.	Kidney.	Testes.
Glycocoll	—	—	—	—	—
Alanin	+	+	+	+	+
Aminobutyric acid	?	?	+	?	+
Aminovalerianic acid	+	+	+	+	+
Leucin	+	+	+	+	+
Glutamic acid	+	+	+	+	+
Aspartic acid	+	+	+	+	+
Pyrrolidin carbonic	?	?	+	+	?
Tyrosin	+	+	+	+	+
Phenylalanin	+	+	+	+	+

A glance at the table shows clearly that the action of the autolytic process in organs is as powerful as that of strong acids combined with high temperature. Nearly all the products which are obtained on prolonged boiling of proteids with strong mineral acids arise also in the course of autolysis. However, there are noted some differences in the two processes. If it be allowed to name substances appearing on cleavage with mineral acid as primary cleavage products, the distinction may be made that on autolysis the primary products undergo further transformation.

On acid cleavage all the amino-acids are obtained which are known to appear on the breaking down of proteid material. Among the end-products of self-digestion of the pancreas, Emerson discovered oxyphenylethylamin, which is not known to be present in the proteid molecule, and which may be regarded as a secondary product derived from tyrosin. Further, on autolysis of various organs the formation of glycocoll was not observed, and prolin could be demonstrated only in a few experiments. It should be remarked that the present methods of analysis of amino-acids are not fully satisfactory and too much weight should not be attached to the results thus far obtained. However, the results of the analysis of the amino-acids obtained from the fresh and from the self-digested glands seem to indicate that

in the course of the latter process some destruction of the substances takes place.

Albumin Metabolism. Falta[1] presents a series of analyses illustrating the destruction of various albumins by the



(1) Deutsches Arch. klin. Med., April, 1906.

body as shown in the nitrogen content of the urine. The appended table shows the percentage of increase over normal of medium quantity and the distribution through the period of destruction of the food applied. The destruction of albumins does not take place with great rapidity. Even the more easily assimilated albumins require a period of three or four days before the reappearance of the N in the urine. The major part of the excretion varies also and in the order of rapidity the principal albumins will take the following order: Gelatin, casein, serum, albumin, fibrin, serum-globulin, hemoglobin, ovo-vitelin, pure egg albumin. In the presence of diseased kidneys the normal curve varies considerably because of the functional insufficiency of these organs. A factor that must be taken into account in these experiments is that relating to the digestibility of the various albumins in the stomach and intestines.

Uric Acid Formation. Mandel[1] deals with all sides of this question, but the point of most general interest is that relating to the seat of uric acid formation. Next in importance to an adequate appreciation of the chemical process by which uric acid originates in metabolism is the recognition of the place where its formation occurs in the organism.

The spleen is still regarded in many text-books as an important factor in the production of uric acid, doubtless owing to the original observation by Horbaczewski on the occurrence of this substance in spleen pulp. The observations of Jackson and Mandel on splenectomized animals, and of Gibson and Mandel on a splenectomized man, have shown that the spleen by no means plays a preëminent rôle in purin metabolism, since both exogenous and endogenous uric acid excretion proceeds undiminished in the absence of that organ. In birds the importance of the liver for the synthesis of uric acid has been exhibited beyond question; but it does not assume an equally significant position in mammals, for a considerable excretion of uric acid continues in animals in which the liver is excluded from the circulation by an Eck fistula.

Summarizing once more the newer observations it ap-

(1) Jour. Amer. Med. Assoc., March 24 and 31, 1906.

pears that especially the spleen, lungs, liver, intestine, muscle and kidney (in some animals at least) are all capable of converting purin bases into uric acid; and that the kidney, muscle and liver can, in turn, further disintegrate the newly formed uric acid—a reaction not accomplished by the spleen or lung. Guanin is first converted into xanthin, which is then oxidized to uric acid; while adenin is first transformed into hypoxanthin from which xanthin subsequently arises. An abundant supply of oxygen is essential in every case, for the change to uric acid and the catalog of effective or inactive organs is presumably not yet complete. Uric acid formation and destruction by no means always proceed together. The uricolytic or destructive ferment is doubtless principally confined to a few distinct organs, especially the kidney and liver.

Digestive System. *Physiology in relation to Medicine and Surgery.* Cannon[1] discusses in detail the bearing that recent studies in the physiology of the digestive organs has upon the progress of medicine and surgery. The ancient axiom that the lungs, heart and brain formed the "tripod of life" ignored the foundation on which the tripod rests. The importance of the activities of the two ends of the stomach is becoming more apparent.

The different appearance of the food in the cardiac and pyloric parts of the stomach was recorded nearly a hundred years ago. This old observation has been newly emphasized by the proof that gastric peristalsis occurs only over the pyloric end of the stomach. The stomach, therefore, is divisible into two parts: a pyloric part, which actively churns the food; and a cardiac part, which is an adaptive reservoir, holding the food without churning it, and opportunely pressing its contents into the pyloric mill.

In the pyloric portion, whenever the pylorus remains closed, the peristaltic rings, moving from the middle to the end of the stomach, push the food into a blind pouch. Since the food cannot then escape through the pylorus, it has, as its only outlet, the opening in the advancing peristaltic rings. As the peristaltic waves recur in rhythmic succession, the food is first advanced and then regurgi-

(1) Amer. Jour. Med. Sc., April, 1906.

tated, over and over again, before it reaches the end of the antrum. When hard masses are brought by the peristaltic waves to the pyloric sphincter, their presence prolongs the period of pyloric closure. Under these circumstances the hard masses are repeatedly swept up to the exit, only to be barred there and shot back through the advancing ring of constriction. By this continual rubbing the waves of peristalsis serve to break up the more solid pieces of food —a function performed by the teeth with manifestly greater efficiency than by the soft gastric mucosa. It seems highly probable that the prevalence of pathological conditions in the pyloric end of the stomach, rather than in the cardiac end—the fact that the pyloric region is the ulcer- and cancer-bearing region—is due to injuries which the greater activity of the pyloric end may bring upon itself.

The repeated squirting of food back through peristaltic rings which are moving up to the pylorus may be used to determine the activity of the gastric musculature. It has recently been shown that when food mixed with air in fine division is eaten this backward squirting of the mixture of air and fluid contents produces a sound. The auscultation of these rhythmic sounds, which normally recur in man at intervals of about twenty seconds, may serve to differentiate between the "motor insufficiency" due to pyloric obstruction and that due to absence of peristalsis.

A number of observations have shown an elective secretion for differing foods. It is therefore possible to change the character of the secretion by regulating the diet.

Among other agents than water, which increase the activity of the gastric glands, meat extract holds a prominent place and justifies its use in clear soups, as the initial course of an extensive meal. Bitters, likewise, may be regarded as stimulants of the secretion, but Pawlow regards their action as due to their primary effects in whetting the appetite. Since it is frequently stated that alkalis and alkaline carbonates produce a rapid flow of gastric juice, it is of interest to note that Pawlow finds an inhibition not only of the gastric but also of the pancreatic secretion after giving sodium bicarbonate. The favorable effects following the use of this salt in cases of hyperacidity he is inclined to attribute to its restraining action on cells that are being overcrowded. Another powerful

inhibitory agent is found in one whole class of foodstuffs, the fats. Fat in the chyme markedly checks the secretory activity of the stomach. Thus fat not digested in the stomach may impede the digestion of proteid food with which it is combined. The use of fatty food, or of fat as an emulsion, in cases of excessive gastric secretion, or of gastric ulcer, seems justified by these experiments, which have proved so strikingly the inhibitory action of fats on the pouring out of pepsin and hydrochloric acid.

The discharge of the digested foods through the pylorus is not simultaneous, but it has been found that, first, starch bodies are discharged, then the proteids, while the fats are passed through slowly.

The seat of the mechanism controlling the remarkable difference in the discharge of the various foodstuffs from the stomach is undoubtedly at the pylorus. The gastric peristaltic waves are most of the time pushing the food against a closed sphincter, thus churning together the food and the gastric juice; and when the sphincter occasionally relaxes these same waves now serve to propel the food into the intestine. What agency causes the pyloric sphincter to relax? It seems probable that the signal for the relaxation is the appearance of free hydrochloric acid in the stomach. For, when acid proteids, on the one hand, and carbohydrates, wet with 1 per cent. sodium bicarbonate, on the other hand, are fed, the acid proteids leave the stomach rapidly like ordinary carbohydrates; whereas, the alkaline carbohydrates, delaying the appearance of free acid, depart slowly after the manner of normal proteids.

In the small intestine secretion is largely dependent upon "secretin." The presence of acid in the duodenum leads to the giving off this substance into the blood and the subsequent activity of the pancreas. This body differs from ordinary enzymes by resisting the action of strong acids.

When the pancreatic juice is secreted it contains no active proteolytic ferment. It seems probable that the other ferments of the pancreatic juice are thus saved from destruction while in the ducts. As soon as the juice reaches the intestine and becomes mixed with the intestinal juice, the trypsinogen of the pure pancreatic secretion, as shown

by Schepowalnikow, is converted by a ferment in the *succus entericus* into trypsin.

The entry of bile into the intestine is regulated in a manner similar to that of the pancreas. As is well known, the bile of a fasting animal is stored in the gall-bladder, and is poured out when the animal has eaten. But the flow begins after different intervals with different kinds of food; neither water, acids, raw egg-albumen, nor boiled starch stimulate the biliary discharge, but fat, as well as extractives of meat and the products of digestion of egg-albumen, set up a free discharge of the fluid. Although acid may not stimulate the flow of bile into the intestine, Bayliss and Starling have found that acid in the duodenum causes a quickened secretion of this fluid, and that secretin injected into the blood-stream has the same effect.

The bile greatly increases the activity of the enzymes of the pancreatic juice. The fat-splitting ferment, for example, has its action increased two to threefold in the presence of bile, and the proteolytic and amyolytic ferments are increased about twofold.

From a surgical standpoint the factors influencing the movements of the stomach and intestines are of great interest.

Recently a study has been made of the effects of etherization, cooling, drying and handling—the various factors concerned in abdominal operations—on the movements of the stomach and intestines. It was found that neither the ether, nor the cooling of the viscera, nor the drying, checked to any marked degree the onward passage of the food. After handling, on the contrary, even the most gentle handling within the peritoneal cavity or under warm salt solution, no gastric peristalsis was seen and no food left the stomach for three hours. Fingering the stomach and intestines gently in air caused still greater retardation of the onward passage of the food; and with rougher handling in air no food passed from the stomach for four hours, and then it emerged very slowly and was moved through the small intestine with extreme sluggishness. These observations were made on normal, vigorous animals; when the strength has been sapped and bodily vigor lost the factors operating to check the activities of the alimentary canal must be much more effective. Noth-

ing is more remarkable than the responsiveness of the canal to conditions of general asthenia, which animals exhibit when afflicted with "distemper." All day long food will lie in the stomach without the slightest sign of a peristaltic wave passing over it. There is a total stoppage of the motor activity of the digestive organs. In asthenic states leading to such conditions the handling of the stomach and intestines can only cause an intensification of the effect of general bodily weakness, a deepening of the state of inactivity.

Cause of Heart Beat. Howell[1] discusses this subject at length and in part says: The immediate cause of the contraction is a chemical reaction or a series of such reactions. In accordance with the knowledge of our day we may assume that the first step in this series consists in the dissociation, the falling into pieces of a complex, unstable molecule, and that this dissociation is followed by an oxidation of the split products. The undoubted necessity of the oxygen for the normal production of a heart contraction may be referred, therefore, to the part that it plays in the second stage of the process, and not to its action as a primary or initial stimulus. The "inner stimulus," if such a thing exists, must be concerned in the production of the initial step of dissociation. We may inaugurate this first step, as is well known, by the application of some external form of energy, such as a mechanical impulse, an electrical current, a nerve impulse, etc., and it is conceivable, of course, that it may be started, as Langendorff and Engelmann have supposed, by some specific substance formed in the metabolism.

The well-nourished heart contains a large supply of energy-yielding material, which is in stable form, so that it neither dissociates spontaneously, nor can be made to do so by the action of external stimuli. It is possible that this stable, non-dissociable form consists of a compound between it and the potassium or the potassium salts, and that herein lies the functional importance of the large amount of potassium contained in the tissue. This compound reacts with the calcium or with the calcium and sodium salts, and a portion of the potassium is replaced

(1) Jour. Am. Med. Assoc., June 9, 1906.

and a compound is formed which is unstable. At the end of the diastolic period this compound reaches a condition of instability such that it dissociates spontaneously, giving rise to the chain of events that culminates in the normal systole. Before spontaneous dissociation occurs it may be hastened prematurely by an external stimulus, as we know to be the case when a mechanical or electrical shock is applied to the heart at any time after diastole has begun.

From this point of view the role of the calcium, or of the calcium and sodium salts, consists in replacing the potassium and converting a part of the store of stable material into an unstable, easily dissociable compound. We are not obliged, therefore, to assume the existence of any specific inner stimulus. An hypothesis of this character accounts readily for some of the most characteristic features of the heart beat.

Heart Block in Mammals. According to the more recent view concerning the path taken by the impulse which normally causes the various chambers of the heart to beat, the impulse arises in the automatically rhythmical musculature of the great veins and is propagated to the various chambers of the heart through their musculature after the nature of a peristalsis. This view is accepted by the upholders of the so-called myogenic theory. Some writers, however, uphold the older, so-called neurogenic theory, according to which the impulse arises in the automatic ganglia of the heart and is distributed to the muscle cells through the medium of nerves.

Until His found a muscular connection between the auricles and the ventricles of the heart, the supporters of the myogenic theory met their greater stumbling-block in the view established by anatomists that in mammals the musculature of the auricular half is completely divided from that of the ventricular half of the heart by connective tissue. With the discovery of the auriculo-ventricular bundle of His, which has been most carefully studied in man by Retzer,[1] the greatest difficulty was removed, but the result of the destruction of this bundle, which represents the only demonstrable myocular connection between auricles and ventricles upon the action of the heart, re-

(1) Arch. f. Anat., 1904, p. 1.

mained to be studied experimentally. It is a *sine qua non* of the myogenic theory that the destruction of the auriculo-ventricular bundle of His should prevent the passage of the impulse from auricles to ventricles. Erlanger[1] undertook such a series of experiments in which he attempted to destroy the connection between the auricles and ventricles by means of a ligature, carried by a fine curved needle, which he passed about the region of the auriculo-ventricular bundle in the heart muscle of dogs. Only in one case out of a total of seven was heart-block obtained by this method. But post-mortem findings showed that this was the only case in which the ligature was so passed as to include the region of His's bundle.

The writer abandoned the ligature as an unreliable method and devised a clamp for the purpose of conducting the experiments and it proved highly satisfactory. With this clamp the writer produced heart-block in every one of many experiments. Simultaneously with the appearance of heart-block the control of the vagus over the ventricles was found to cease in almost every instance.

These experiments led the writer to conclude positively that the impulse which causes normally the ventricles to act is conducted through the auriculo-ventricular bundle of His.

All stages of heart-block were obtained by the writer upon compression. These include:

1. An increase of the intersystolic pause.
2. An occasional ventricular silence.
3. Regularly recurring ventricular silences—e. g., one silence in ten, nine, eight, seven, six, five, four, three and two auricular beats.
4. A 2:1 rhythm.
5. A 3:1 rhythm.
6. Complete heart-block.

At the moment when complete heart-block is established the ventricles generally take on a slow rate. At times a marked preliminary slowing of the ventricular rate may be observed; such is usually the case when the block becomes complete suddenly.

When the block is complete stimulation of the vagus

(1) Jour. of Exp. Med., vol. VIII, No. 1, Jan. 25, 1906.

nerve has no, or but a minimal, effect upon the rate and force of the ventricular beats, whereas the auricles still react normally; stimulation of the accelerator nerve increases the rate both of the auricles and the ventricles.

When the block is complete, the rate of ventricular beats may not be materially affected by variations in the general blood pressure, nor by asphyxia, nor by interference with the coronary circulation.

Heart Block and Stokes-Adams Disease. The cardinal symptoms of Stokes-Adams disease were recognized by Stokes[1] and are enumerated by Erlanger, in the work referred to above, as follows:

1. A slow pulse sometimes associated with pulsation in the veins of the neck, which may be more than twice as frequent as the manifest beats of the ventricles.

2. Syncopal attacks which may be epileptiform or apoplectiform in character and in which the pulse rate is unusually slow.

Based upon his experimental causation of heart-block, Erlanger maintains that a lesion in the vicinity of the auriculo-ventricular bundle may account for all the typical symptoms of Stokes-Adams disease. In other words, heart-block and its attendant phenomena may duplicate all the cardinal symptoms of Stokes-Adams disease. The writer maintains, furthermore, that in every reported case of Stokes-Adams disease the diagnosis of heart-block would have been reached if the tracings had been properly interpreted. At any rate, he notes that the description of the cases as found in literature does not preclude the existence of heart-block in one single instance. Indeed, the data given are sufficient in many instances to justify a diagnosis of heart-block, and it is more than a coincidence that the first demonstrated instance of heart-block, reported by Chaveau,[2] had been diagnosed a case of Stokes-Adams disease one year previously by Figuet,[3] who described it as a typical instance of "rythme couplé." Erlanger concludes from his studies that heart-block is always the cause of Stokes-Adams disease. He inclines to

(1) Dublin Quart. Jour. of Med. Sc., 1846, II, p. 73.
(2) Rev. de Méd., 1885, vol. V, p. 161.
(3) Thesis, Lyon, 1882.

look upon heart-block with and without syncopal attacks as different stages of the same disease process.

The Blood Plates. The elaborate article on the blood plates by Kemp, Calhoun and Harris[1] deals with methods and original observations. The following considerations that may be of value in diagnosis and prognosis are presented:

Acute Infectious Fevers.—During the course of an acute infectious fever (especially typhoid) the number of blood plates is usually either subnormal or normal. If the fever breaks by crisis, the crisis is accompanied by a rapid and striking rise in the number of blood plates. This is the classical "crise hématique" or "crise hématoblastique" of Hayem. If this "crise hématique" fails to appear, it is the sign of some masked complication which is usually unfavorable. Most observers have found that this is true of all acute infectious diseases, but all are practically agreed on typhoid. The study of the plates in pneumonia has been especially interesting. As a rule, observers have found a marked blood crisis, but they are not in accord as to whether the plates are increased or diminished during the continuance of the fever. On some other fevers there has been a wider divergence of opinion. The study of the leucocytes in fevers has attracted considerable attention. Further investigations on the blood plates in fevers would lead to valuable results, besides being of use in diagnosis and prognosis for the cases under observation.

Anæmias.—In the different anemias, there is a remarkable concurrence of opinion that the plates may or may not be diminished in secondary anemias—indeed, in most cases, they are reported to be increased; while in pernicious anemia they are always greatly diminished. An increase above the normal in the number of the blood plates excludes the diagnosis of pernicious anemia. If a case under treatment shows an increase in the number of the blood plates, the prognosis is encouraging; if, in spite of all that can be done, the plates continue to fall in number, the prognosis is almost certainly fatal. In this connection we can not do better than quote from the

(1) Jour. Med. Assoc., April 14, 1906.

latest work of the veteran observer Hayem, who speaks with especial emphasis on the study of blood plates in anemias. He says: "It is certainly wrong to neglect these elements. When their number becomes small it is always a more or less serious sign; when they become rare the retractability of the clot diminishes. . . . This double lesion rarity of the hematoblasts [blood plates] and loss of retractability of the clot is a sign of progressive pernicious anemia, and is the most characteristic sign which we have of this protopathic form. If this double sign does not exist, the proper treatment will effect a cure, and one of the first signs of improvement is a rise in the number of blood plates. If the case continues to improve, further interesting changes are noted in the relation of the plates to the red corpuscles; small red corpuscles appear in increasing numbers and there is every indication that young red corpuscles are developed from the plates. Hayem's observations, so far as the numerical relations of the blood plates are concerned, have been confirmed by a number of observers, including van Emden and Pratt, whose methods of numeration are free from the objections which apply to the older method of Hayem.

Purpura Hemorrhagica.—In *Purpura hemorrhagica* the number of blood plates is enormously diminished. Van Emden and Pratt each state that the lowest counts they have ever found have been in this disease. Hayem called attention to the slowness in clotting of the blood. Helber confirms this observation of Hayem. To distinguish the blood in *Purpura hemorrhagica* from that of pernicious anemia, Hayem says that, in the absence of appreciable changes in form in the red corpuscles, "the scarcity of hematoblasts [blood plates] and the absence of serum after the coagulation of the blood, are two signs which are constant and pathognomonic" of the disease. The few plates which are found are often of large size. The blood contains masses of small plates, but these are broken down. Fibrin threads in the clot are few, but coarse. Recovery is ushered in by a "crise hématoblastique."

Physiology of Prostate. Jappelle and Scafa[1] removed

(1) Arch. Ital. de Biol., May, 1906.

the prostate gland in dogs and injected an extract made therefrom into other dogs. Such an extract is very toxic when injected into the veins and causes paralysis of the respiratory center and a decided increase in the blood pressure. There is also interference with the coagulation of the blood. Some toleration to the injection may develop but the inhibitory action upon the respiratory centers may become so sudden that the animal may die.

Absorption by the Peritoneal Cavity. Buxton and Torrey[1] find that almost immediately after the injection of inert particles into the peritoneal cavity of a guinea-pig there is a deposit of fibrin on the surface of the omentum in which the particles and the phagocytic cells become entangled. Small particles like lamp black become englobed by phagocytes within ten minutes and such particles as chicken corpuscles in about an hour. If the phagocytes are not overloaded they pass into the tissues and appear as long trailers or clasmatocytes. If the particles are digestible they are rapidly disposed of by the phagocytes. The macrophages are the most active phagocytes. The omentum takes a most important part in the disposition of either particles or bacteria that arrive in the peritoneal cavity. When typhoid bacilli are injected into a rabbit they become fixed in great numbers on the surface of the omentum. Some may lie free in the fibrinous deposit, some may be contained in macrophages. The destruction of the bacilli takes place both extra- and intra-cellularly. At times they remain intact on the surface for a considerable period. When they are rapidly destroyed there is a good microxycyte reaction in four to six hours. If the microxycytes fail to appear in large numbers secondary centers of multiplication appear. If the rabbit is recovering these secondary centers disappear in 16—24 hours. The macrophages are the chief agents in phagocytosis, but they are not entirely effective unless there is a considerable microxycyte reaction.

(1) Jour. Am. Med. Assoc., April 14, 1906.

SECTION III.

GENERAL PATHOLOGY.

METHODS—MICROSCOPIC DIAGNOSIS.

Ra id Diagnosis of Rabies. When it is possible L. Frothingham[1] recommends that the specimens be fixed imbedded, cut and stained. The areas selected are the Ammon's horn, the hippocampus major,—from the cerebellum. Following is the technique:

(1) Small pieces of Ammon's horn and of gasserian ganglion are placed in Zenkers' fluid for four hours; (2) ninety-five per cent. alcohol for several hours; (3) absolute alcohol, one-half hour; (4) absolute alcohol and chloroform, equal parts, 20 to 30 minutes; (5) chloroform 20 to 30 minutes; (6) chloroform and paraffin saturated solution, warm, 20 to 30 minutes; (7) paraffin at 55° C. 30 minutes; (8) imbed; (9) cut; (10) float sections on water at 40° C. and fix on slide with glycerin albumen; (11) 30 minutes at 55° C.; (12) xylol, to remove paraffin; (13) absolute alcohol; (14) 95 per cent. alcohol; (15) saturated alcoholic solution of iodin, 5 to 10 minutes; (16) wash out iodin with 95 per cent. alcohol; (17) wash in water; (18) stain 15 to 30 minutes in equal parts Unna's stain, 5 per cent. aqueous eosin (Grubler, W. G.); (19) wash in water; (20) Unna's stain, 3 to 5 minutes; (21) water; (22) differentiate in 95 per cent. alcohol until desired color is obtained (using microscope from time to time); (23) absolute alcohol; (24) xylol; (25) balsam.

Another method recommended by Frothingham is as follows: Sections are (1) dried in the air; (2) 95 per cent. alcohol, 10 minutes; (3) iodin solution, 10 minutes; (4)

(1) Jour. Med. Research, April, 1906.

95 per cent. alcohol, 10 minutes; (5) water; (6) stain as above. Or, sections are (1) dried and fixed with gentle heat; (2) saturated alcoholic eosin, 15 minutes; (3) wash in water; (4) Löffler's alkaline methylen blue, 3 to 5 minutes; (5) wash in water; (6) differentiate in 95 per cent. alcohol; clear, mount, etc. Frothingham recommends these methods in the order given.

Results of Frothingham's stains: Nucleolus stains dark blue; cell body and nucleus, pale blue; red blood corpuscles, brilliant pink; Negri bodies, extracellular and intracellular, a peculiar pink color, often with colorless or blue internal markings of various shapes and sizes. He says the bodies stain well with Mallory's iron hematoxylin. He has not had good results with Mann's method.

Frothingham's method for rapid examination: (1) Dissect out Ammon's horn and, cutting with scissors at right angles to its length, divide it into small disks; (2) press a thoroughly cleaned slide upon a disk and remove it suddenly; make four to eight impressions on one slide; (3) before the impressions have thoroughly dried place them in Zenkers' fluid 30 minutes to 2 hours; (4) wash in water; (5) 95 per cent. alcohol, 5 to 10 minutes; (6) saturated alcoholic solution iodin, 5 to 10 minutes; (7) wash out with 95 per cent. alcohol; (8) wash in water; (9) stain as described above.

Significance of Casts in the Urine. Emerson[1] estimates the significance of casts in the urine as follows:

Cylindruria is the presence of casts in the urine. It is "pure" if no albumen is present as tested by the ordinary clinical tests. *Varieties:* Epithelial casts are made up of cells with round nuclei. They are parts of the tubules below the loops of Henle and some have lumina which can be seen. In addition to these, and classed under the same name, are hyaline casts with one, two, or a few cells with round nuclei attached. Many of these cells have a perfectly clear protoplasm, though the kidney cells are granular. Those of the first type are rare. They occur in acute nephritis. Those of the second type are common. They can be found in bicycle riders and athletes, as can blood casts, not uncommonly after hard exercise, *i. e.*,

(1) Johns Hopkins Hosp. Bull., Jan., 1906.

hyaline casts with a few blood cells attached. Blood casts which are clots of blood occur in hemorrhagic nephritis. A true pus cast occurs in purulent nephritis, but hyaline casts with pus cells attached are found in athletes. Coarsely granular casts are opaque with very coarse granules. They are not translucent and evidently are pus or epithelial casts gone to pieces. The next stage in the degeneration of this form is the waxy cast which occurs in two varieties, white and yellow, both of which tend to split transversely. The true hyaline cast is faint and watery and is seen only by shutting off the light. It may be found wherever albumin is expected and does not stain by iodin. There is a cast usually called hyaline, though it is not, which is not so refractile as the waxy casts, occurs in nephritis or long-standing renal trouble, and stands between the waxy and hyaline groups. Associated with this intermediate group are very translucent fine granular casts. The waxy casts are the modified granular casts. These may be found in the last few c.c. of urine secreted before death, even though they were not formerly present. Also one can find waxy casts of all stages in the tubules. Fatty casts are covered by globules of fat. In the last five years every case with fine fatty casts in the Johns Hopkins Hospital was of malarial nephritis. However, often in nephritis the renal cells will be swollen with fat globules and all transitions between rows of single cells and fatty casts can be seen. There may be globules of myelin degeneration in the cells. These do not take osmic acid and may form a true myelin cast.

The autopsy records of all cases with a clinical diagnosis of nephritis, also the clinical records of all with an anatomical diagnosis of nephritis were studied. In some cases of chronic passive congestion with a clinical diagnosis of nephritis, but no anatomical evidences, there were all varieties of casts. In some cases of cloudy swelling where there had been all varieties of casts there were no evidences of nephritis. Cases with fatty kidneys had been diagnosed nephritis. One hundred cases of acute nephritis were studied. The diagnosis cannot be made from the urine alone, for acute nephritis and exacerbations of chronic nephritis cannot be thus distinguished. To make a diagnosis of acute parenchymatous nephritis, one

must also have a history of the patient. Of chronic interstitial nephritis there were two types, the white kidneys and the red kidneys, the latter due chiefly to arteriosclerosis. In the cases of small red kidney the trace of albumin often persists longer than the casts which often disappeared first. In the small white type the albumin often clears up first. Of eighteen cases of amyloid kidney only one-fourth had large amounts of urine and albumin but very few casts. The more acute the attack, the more epithelial, blood, and pus casts are present. In the chronic attacks these diminish and are replaced by waxy, hyaline and granular casts. These cases can be followed by the casts alone.

Pure cylindruria occurs oftener than is generally supposed if the urine is examined fresh, centrifuged, and carefully studied. A slight circulatory disturbance of the kidneys, or manipulation as bimanual palpation, may cause casts and no albumin, or the reverse, or both. The cases of chronic nephritis with history of small white kidney may have casts with no albumin.

Pure cylindruria may follow the use of drugs, *e. g.*, sodium salicylate, though the casts disappear as soon as the medicine is stopped. Alcohol in moderate doses will cause cylindruria in over one-half the cases; in others albuminuria. Ung. hydrarg. also may cause the presence of casts. Many of the acute diseases, as erysipelas, scarlet fever, tonsillitis and diphtheria, show the symptoms of nephritis, but in some cases only casts can be found. The point to be emphasized is that the number of such cases is large.

"Showers" of casts may herald oncoming diabetic coma, sometimes without albumin; they appear suddenly. There are few epithelial or waxy casts, but those present are hyaline or finely granular. These showers occur in exacerbations of nephritis, after diuretics, or, as a terminal event, the last two or three days before death. In chronic constipation there may be found a pure cylindruria. It is an inflammatory or irritative process, not a degeneration, that causes casts. The greatest number of casts is produced by kidneys which are but slightly diseased or by the disturbance of a normal cortex, fewer by a small granular kidney, and the least number when the cortex is most

extensively diseased. The more normal the cell the better its cast-producing ability. The number and kind of casts are indications of the present condition of kidney epithelium. The specimen should be centrifuged and examined carefully immediately after voiding. Epithelial, blood, and pus casts do not have as much significance as generally supposed. Cells of casts should be studied to determine whether they are epithelial or pus cells, for these casts are certainly present more often than recorded.

A New Very Sensitive Agent for Albumin in the Urine. A. Tognetti[1] describes his method as follows: Add to the urine an equal quantity of alcoholic solution of tannin (1.5 grams of tannin in 100 c.c. 90 per cent. alcohol). Heat, and then add one-half the quantity of 33 per cent. HCl in water. If albumin is present a yellowish white precipitate is formed. If jaundice is present the bile must be removed first by the Grocco method, namely, addition of glacial acetic acid in the proportion of 1/30 to 1/50 the volume of urine. This test for albumin is very delicate and is not disturbed by anything except bile.

Practical Significance of a Trace of Albumin in the Urine. Tunis,[2] while freely admitting the existence of a condition frequently termed physiologic albuminuria, thinks the term a bad one. Cases showing a trace of albumin and no casts are prone to eventually develop true nephritis. The prompt means of discriminating between the transient forms of albuminuria and those of real clinical significance may be found in some such therapeutic test as that of calcium lactate rather than by any further developments in the chemistry of the urine. Wright and Ross[3] do not agree that it is always necessary to take a serious view of physiologic albuminuria. It is their opinion that in physiologic albuminuria there is a transudation of serum from the lymph channels of the kidney into healthy tubules. They give 40 to 60 grains of calcium lactate to cases of physiologic and pathologic albuminuria. In the former the albumin disappeared from the urine. In the latter it did not. The coagulating time of the blood was taken before the calcium salt was administered

(1) Gazetta degli Ospedali, Milan, vol. XXVII, No. 51.
(2) Amer. Jour. Med. Sc., July, 1906.
(3) Lancet, Oct. 21, 1905.

and again at intervals from one to twenty-four hours afterward. The usual decrease in the coagulation period was about thirty seconds. The urine was examined at the same periods. The albumin either disappeared or was markedly decreased. In the cases of pathologic albuminuria there was the same decrease in the coagulating time of the blood but there was no change in the quantity of albumin in the urine. Wright and Ross advocate this as a method of differentiating all forms of non-inflammatory nephritis from those which are inflammatory. As a further means of differentiation they offer the excretory quotient. This method Wright and Ross offer as a substitute for cryoscopy, saying that in addition to necessitating less apparatus it requires less technical skill. In physiologic albuminuria they found an excretory quotient ranging from 2 to 3.5 and averaging 2.3, whereas in pathologic albuminuria the excretory quotient ranged from 0.5 to 1.4 and averaged 0.9.

Essential Pentosuria in Two Brothers. Janeway[1] divides pentosurias into three groups: (1) Alimentary pentosuria; (2) diabetic pentosuria; (3) essential pentosuria. The first group is composed of those transient cases in which the pentose shows on the polariscope. The second group is merely a variation in an extreme degree of ordinary diabetes. In the third we find true pentose. It is optically inactive, gives a phenylhydrogen reaction, a delayed Fehling test and a bubble or two of gas on fermentation. It is not affected by diet and seems to be but little related to other forms of diabetes. It appears especially in neurotic people. It is not infrequent that more than one member of a family is afflicted. The orcin test is satisfactory when performed with restrictions suggested by Brat (Zeit. f. klin. Med., 1902, Vol. XLVII, p. 499). To 3 c.c. of urine add 5 c.c. concentrated HCl, sp. gr. 1.19, and a knife point full of orcin. If the urine is concentrated, dilute before using. Heat carefully on a water bath to 90 to 95° C. for two or three minutes. If pentose is present a green precipitate forms. Take this up with amyl alcohol and examine spectroscopically. An absorption band in the orange and contiguous red is typical of pentose.

(1) Amer. Jour. Med. Sc., Sept., 1906.

Examination of the Urine for Lead. Leverer[1] describes a method of examination of the urine for lead for which he claims accuracy, rapidity and simplicity. It is as follows: Five hundred c.c. of urine is placed in a lead-free dish and 70 c.c. of pure concentrated H_2SO_4 is added. Heat carefully over a Bunsen burner. Add 20 to 25 grams of potassium persulphate. The mixture is concentrated to 250 c.c. Should it become cloudy add a small amount of sulphuric acid. If it darkens add a few grains of the persulphate. Let the mixture cool and add 250 c.c. of alcohol (90 vol. per cent.). Allow the mixture to stand for four hours in a cool place. The lead precipitates as an insoluble sulphate. Filter through a quantitative filter paper. Wash with hydrochloric acid and then with fluoric acid and wash out the dish with alcohol and run the washing through the filter. Now punch a small hole in the filter paper with a clean rod. Wash off the filter paper and rod with about 10 c.c. of distilled water. Take this water, heat over a Bunsen burner and add crystals of sodium acetate until the solution is clear and transparent. Cool. Pass hydrogen sulphide through the water; a yellowish brown discoloration means lead. Pass some hydrogen sulphide through distilled water as a check. The quantity can be determined by comparing with solutions of lead of a known strength. Lederer found the test accurate for 0.00002 grams of lead.

Sahli's Desmoid Reaction in Gastric Diagnosis. Boggs[2] describes the Sahli's method as follows: The pill consists of 0.05 gram of methylen blue and 0.1 gram iodoform, with just enough licorice to make a mass not to exceed 3 to 4 mm. in diameter. This pill is enclosed in a piece of thin rubber dam, the neck twisted and tied with three turns of 00 raw catgut, previously soaked in cold water until soft. The edges of the rubber are trimmed. The rubber must not stick together and the gut must be securely knotted. Finally, the bag must not leak when submerged in water. The pill is taken just after the midday meal and the urine is collected 5, 7 and 20 hours later and tested for blue and iodin. The urine may be greenish blue or if not, and methylen is present, boiling with

(1) Jour. Am. Med. Assoc., July 14, 1906.
(2) Johns Hopkins Hosp. Bulletin, Sept., 1906.

one-third volume of glacial acetic acid will develop it. To detect iodin strongly acidify the urine with HNO_3 and shake out with chloroform when a rose color appears. If the color of the iodin appears in 20 hours the reaction is positive, otherwise it is negative. The principle of the test is that catgut is soluble in gastric juice but not in pancreatic juice or intestinal secretion.

Boggs thinks that its chief value is as a test for free HCl. He does not agree with Kaleski (Deut. med. Woch., 1906, p. 185), that deductions as to degree of involvement can be drawn from the rapidity of the appearance of the drugs in the urine. He studied forty-six cases in conjunction with analyses of the stomach contents. His conclusion is that it can never replace stomach analyses, but in all cases it furnishes good collateral evidence and in those cases in which it is impossible to empty the stomach with a tube the test is of great value.

Einhorn (Jour. Amer. Med. Assoc., May 12, 1906) does not think the test of any value because catgut is dissolved in the intestines as well as in the stomach. This he has demonstrated experimentally. In addition he used it on four cases of achylia gastrica, one of which was due to carcinoma, and got a reaction in from 4 to 18 hours in the different cases.

Boggs thought Einhorn's conclusions unjustified because his facts were too few.

Notes on Clinical Examination of Feces. J. Dutton Steele[1] says that in a case in which there is a large amount of muscle fiber in the stools there may be either a lack of trypsinogen or of its activating ferment enterokinase,—the latter a secretion of the intestinal glands. A small amount of muscle fiber is of no clinical significance. He cites a case of chronic appendicitis in which there was a diarrhea coming on whenever red meat was given as a food. Whenever 200 grams of meat was given muscle fiber in the stool could be recognized with the naked eye. No nuclei could be seen in the meat with the microscope. Starch and fat digestion and absorption were good. Gastric

(1) Jour. Amer. Med. Assoc., May 12, 1906.

secretion and digestion were good. Diarrhea ceased when meat was stopped, to reappear upon taking of meat. After removal of the appendix the intestines gained their power to digest meat. There was a re-establishment of the secretion of enterokinase. He reports a second and very similar case in nearly every detail. The stools showed some fatty soap crystals but no neutral fats. Starches were always well handled. The muscle fiber was abundant but there was not much muscular putrefaction. There were no nuclei in the muscle fibers. Stomach secretion and digestion was good. Hydrobilerubin present. No blood—occult or other. No mucus. The patient improved in every particular on a diet of starch and fat, with a minimum of proteids. There was always recurrence of diarrhea upon the taking of meat. After the appendix was removed the patient regained his power to digest meat.

Occult Bleeding in Typhoid Fever. Petroske and Ramoni[1] say that in their experience occult bleeding in typhoid fever always preceded bleeding visible to the naked eye by from one to five days. By systematic examination then of the feces in typhoid fever serious hemorrhage could be foreseen and guarded against. The clinical importance of this observation can be readily understood and it is greatly to be regretted that Steele was not able to verify their conclusions. He found that occult bleeding in typhoid fever was not very frequent. In fact, the typhoid ulcer has less disposition to bleed than any other ulcer in the gastrointestinal tract. In his experience occult bleeding did not precede visible hemorrhage with sufficient regularity to make routine examination very profitable. Occult bleeding occurred in his mild cases as often as in those which were severe. On the other hand the cases of visible hemorrhage were preceded by days of occult bleeding. In other words, while occult bleeding preceded visible hemorrhage no conclusions relating to hemorrhage or as to the severity of the disease could be drawn from the finding of occult blood.

The writer made use of Klunge and Schaer's test for the detection of blood; the technique of this method, as reported in Vol. IX of last year's Practical Medicine series,

(1) Univ. Pa. Medical Bulletin, July, 1906.

is as follows: Mix 5 grams of feces with enough distilled water to make semiliquid. Then thoroughly mix with an equal volume of ether, shake well, allow to stand for fifteen minutes, and then pour off the supernatant liquid. Mix the residue with one-third its volume of glacial acetic acid and then add 10 c.c. of ether. Shake well, allow to stand for fifteen minutes. The ethereal extract will rise to top as a clear liquid and can be poured off.

Take as much aloin as will go on the end of a spatula. Place in one-third of a test tube of 70 per cent. alcohol.

To use: Two to 3 c.c. of the clear yellow aloin solution is mixed in a test tube with the same amount of the ethereal acetic acid extract and 2 to 3 c.c. of ozonized turpentine is added and the whole gently shaken. The mixture should develop color in fifteen minutes. If more time is given a color not due to blood will appear. The reaction may show in several ways: Either the whole mixture turns pink and then cherry red, or the aloin sinks to the bottom and forms a layer which becomes gradually a deep cherry red, or, if the aloin is allowed to flow gently down into the turpentine-ether-extract mixture, a deep red ring is given.

The aloin solution must be freshly made. The ozonized oil is made by allowing a c. p. oil of turpentine to stand for at least three weeks.

Weber's Test.[1] Shake a gram or so of gum guaiac in a test tube half full of ether, allow it to stand until it settles clear. Take 2 c.c. of the guaiac mixture and 2 c.c. of ether-acetic extract of feces and an equal quantity of hydrogen peroxid; shake well. The olive color quickly appears in the top portion. The guaiac must be freshly made.

Some of the shortcomings of these delicate tests are: a full meal of rare red meats will give it. Well cooked fish, fowl, ham or kidney will not give it. A diet of pressed beef juice will not give it. Vegetables will not disturb the aloin reaction. They sometimes make it difficult to judge the guaiac reaction. The taking of iron by the patient never interfered with the test. Care must be taken with regard to blood from innocent sources; *e. g.*,

(1) Berl. klin. Woch., 1893, No. 19.

hemoptysis, epistaxis, hemorrhoids, fissures, menstruation, etc.

Examination of the Urine and Feces in Diseases of the Pancreas. Cammidge,[1] in 1904, published some methods of examination of the urine and feces through the use of which he and Mayo Robson had been able to get better clinical ideas as to pancreatic conditions. These tests were rather empirical and not very satisfying to the general reader. He now announces improvement in his technique as follows: A preliminary examination of the urine is made for albumin, sugar, bile, urobilin and indican, a quantitative examination for chlorids, phosphates and urea, and a microscopic examination for oxalate crystals. If found to be free from albumin and sugar and acid in reaction, take 1 c.c. strong HCl (specific gravity, 1.16), mix with 20 c.c. clear filtered urine and gently boil on a sand bath in a flask, using a funnel as a condensor and stopper. After 10 minutes' boiling, cool the flask in a stream of water, and increase the contents up to 20 c.c. with cold distilled water. "The excess of acid present is neutralized by slowly adding four grams of lead carbonate. After standing for a few minutes to allow of the completion of the reaction, the flask is cooled in running water, and the contents filtered through a well-moistened close-grained filter-paper until a perfectly clear filtrate is obtained. The filtrate is then well shaken with 4 grams of powdered tribasic lead acetate, and the resulting precipitate removed by careful filtration, an absolutely clear filtrate being secured by repeating the filtration several times if necessary. Since the large amount of lead now in solution would interfere with the subsequent steps of the experiment, it is removed with a stream of sulphuretted hydrogen, or, what I have found equally satisfactory and less disagreeable, by precipitating the lead as a sulphate. For this purpose the clear filtrate is well shaken with 2 grams of powdered sodium sulphate, the mixture heated to the boiling point, then cooled in a stream of water and the white precipitate removed by careful filtration; 10 c.c. of the perfectly clear transparent filtrate is made up to 18 c.c. with distilled water and added to 8 grams of

(1) Surgery, Gynecology and Obstetrics, September, 1906.

phenylhydrazin hydrochlorate, 2 grams of powdered sodium acetate, and 1 c.c. of 50 per cent. acetic acid contained in a small flask fitted with a funnel condenser. The mixture is boiled on a sand-bath for ten minutes and then filtered hot through a filter-paper moistened with hot water into a test-tube provided with a 15 c.c. mark. Should the filtrate fail to reach the mark, it is made up to 15 c.c. with hot distilled water, but in my own work I rarely find this is necessary, for with practice it is possible to so regulate the boiling that the final result always comes out between 15 and 16 c.c. In well-marked cases of pancreatic inflammation, a light yellow flocculent precipitate should form in a few hours, but in less advanced cases it may be necessary to allow the preparation to stand overnight before a deposit appears. Under the microscope the precipitate is seen to consist of long, light yellow, flexible hair-like crystals, which, when irrigated with 33 per cent. sulphuric acid, melt away and disappear in 10 to 15 seconds after the acid first touches them. The precipitate must always be examined microscopically, as it may be difficult to determine the characters of a small deposit with the naked eye, and so cases giving only a slight reaction may be overlooked. To exclude traces of sugar undetected by the preliminary reduction tests, a control experiment is carried out by treating 20 c.c. of the urine in the same way as in the test described, excepting for the addition of the hydrochloric acid. Any sugar found to be present may be removed by fermentation with yeast after the urine has been boiled with the acid and neutralized. It is essential for the success of the test that the urine should be fresh and not have undergone fermentative changes. If it should be alkaline in reaction, it must be acidified with hydrochloric acid before the experiment is commenced. It has also been found that the administration of calcium chloride as Mr. Mayo Robson recommends before operation in pancreatic cases, interferes with the reaction in the urine.

"My experience with the improved method has been most satisfactory, for in every case where pancreatitis has been found to be present, the urine has given a more or less marked reaction, corresponding to the extent of the lesion. In several cases which gave a well-marked reaction, I have

had the opportunity of re-examining the urine after operation, at intervals ranging from one to six months, and in every instance with a negative result. Normal urines have given no reaction, and control cases suffering from cancer of the stomach, colon, or rectum, and from gastric ulcer, duodenal ulcer, gastritis, colitis, appendicitis, tuberculosis of the intestine, intestinal obstruction, cirrhosis of the liver, hepatic abscess, nephritis, floating kidney, tuberculosis of the kidney, cystitis, and Addison's disease, etc., where there was no pancreatic lesion, have also proved negative. The urine from cases of cancer of the pancreas has generally given no reaction, but in about 25 per cent. of the cases I have examined, a more or less marked deposit of crystals was secured. The crystals had no special distinguishing characters, and appeared to be of the same nature as those obtained in ordinary cases of pancreatic inflammation. The explanation probably is that they are due to an inflammatory reaction set up in the unaffected portion of the pancreas by a rapidly invading new growth. The possibility of a pancreatitis secondary to malignant disease has always to be borne in mind when the urine yields a positive result by this method, especially if it is loaded with bile, is poor in chlorides, and gives a reaction with ferric chloride. In these cases a preparation made by the original *'a'* method, previously described, will often assist in forming a correct opinion.

"In many cases of pancreatitis, and in most of cancer of the head of the pancreas, useful confirmatory evidence may be obtained by an examination of the feces. My procedure is, after noticing the naked-eye characters, to make a careful microscopical investigation of specimens taken from various parts of the sample for fat globules, fat crystals, muscle fibers, inorganic crystals, etc.; then to take the reaction to litmus of a portion selected from the center of the mass, and subsequently to estimate the percentage of 'total fat,' 'neutral fat,' and 'fatty acids' in a specimen dried to a constant weight on the water bath. Finally, an examination for stercobilin is made. For the estimation of the fats I have adopted a method which, while much more rapid than the Soxhlet process, gives results that are satisfactory for clinical work. It may be briefly described as follows: Two clean dry Schmidt-

Stokes milk-tubes (labeled A and B), and provided with a 10 c.c. mark, are taken. Into the lower bulb of each is introduced an accurately weighed quantity of the finely powdered dried feces. I usually employ about half a gram. The residue on the watch-glass used for weighing, and on the sides of the short-necked funnel with which the powder is introduced into the tube, is washed down with a fine jet from a wash-bottle, which for the A tube contains hydrochloric acid (1 in 3) and for the B tube water. The sides of the tubes are also washed down until the whole of the sample is collected into the lower bulb and the 10 c.c. mark is reached. The A tube is then heated in boiling water for half an hour, occasionally rotating it so as to well mix the contents. After cooling, both tubes are filled to the 50 c.c. mark with ether, securely corked, and inverted forty or fifty times, allowing the whole of the solid material to run through the ether each time. Each tube is then rotated between the hands, fixed in an upright position, and left undisturbed for half an hour or more, so that the whole of the solid residue may be brought into the lower bulb. Considerable care is required in this part of the operation, or a perfectly clear supernatant layer of ether free from solid may not be secured. With a pipette, exactly 20 c.c. of the ethereal extract is drawn off from each tube and delivered into two CO_2 flasks of known weight, the amount of ether in the tubes being at the same time read off. The ether in the flasks is evaporated off, the residue dried on a water bath, and the flasks again weighed. From the amount of extract yielded by 20 c.c. of ether, and the quantity of ether left in the tubes, the total amount obtained from the weight of dried feces used may be calculated, and from this the percentage in the stool determined. For convenience of reference I am in the habit of describing the yield from the A tube as 'total fat,' that from the B tube as 'neutral fat,' and the difference between the two as 'fatty acids.' The solid residue in the B tube can be used for detecting stercobilin. For this purpose it is filtered off, extracted with acid alcohol, neutralized with ammonia, and an equal quantity of 10 per cent. zinc acetate in alcohol added. The precipitate which forms is removed by filtration, and the clear filtrate examined against a black background for the green fluorescence

which indicates the presence of stercobilin. The intensity of the color varies with the amount of pigment, so that by always using approximately the same quantities of feces and of the reagents, any marked variation from the normal can be detected.

"The color of the stools may vary from the typical dead white of cancer of the head of the pancreas and advanced pancreatitis to an approximately normal appearance in the slighter cases of pancreatic inflammation. When the pancreas is diseased, the feces generally have an acid reaction, while in cases of simple biliary obstruction, not associated with a pancreatic lesion, the reaction is alkaline. This is not, however, an absolute rule, for in 10 per cent. of the cancer cases I have examined, the feces were alkaline, and red litmus was turned a more or less deep blue in about 35 per cent. of the cases of chronic pancreatitis investigated. In practically all cases of simple pancreatitis, stercobilin can be found in the feces, although in some instances where the pancreatic inflammation is associated with recent obstruction of the common duct by a biliary calculus, only traces can be detected. Even traces of stercobilin are uncommon in cancer of the head of the pancreas, at least at the stage at which they usually come under observation. Determination of the nitrogen content of the feces has not in my hands proven of much value as an aid to diagnosis, but the discovery of large numbers of undigested muscle fibers with the microscope is a useful indication of malignant disease or of advanced inflammatory trouble. Microscopically, too, crowds of fat globules and fatty acid crystals are always to be found in serious cases of pancreatic disease. Quantitative estimation of the 'total fat' gives results that are always above the normal in cancer of the pancreas, the average in my cases being 63 per cent., with extremes of 40 and 90 per cent. The 'neutral fat' in the cases I have examined has varied from 40 to 60 per cent., the average being 45 per cent. The 'fatty acids' have ranged from 9 to 33 per cent., the mean being 18 per cent. of the dry weight of the feces. In chronic pancreatitis, similar but usually less marked variations from the normal are met with. The 'total fat' rarely exceeds 60 per cent., and may fall within the normal limits for a mixed diet of 15 to 25 per cent. The relation

of the 'neutral fats' to the 'fatty acids,' which are normally present in about equal proportions, is frequently disturbed, especially in well-marked cases of inflammation of the pancreas, the neutral fats being in excess. The average proportion in my cases has been 32 per cent. of 'neutral fat' to 18 per cent. of 'fatty acid.' In cases of biliary obstruction, not associated with pancreatic disease, although the percentage of 'total fat' is often in excess of the normal, and the relation of the 'neutral fats' to the 'fatty acids' is disturbed, the tendency being for the latter to preponderate. The average amounts in the cases I have investigated have been 49 per cent. for the 'total fats,' 18 per cent. for the 'neutral fats,' and 23 per cent. for the fatty acids. Taken alone, an analysis of the feces cannot be considered a reliable indication of the condition of the pancreas; but as confirmatory evidence of the results of an examination of the urine, it is of considerable value, especially in suspended cases of malignant disease.

"My experience on the pathological side and that of Mr. Mayo Robson on the clinical have shown that the probabilities of an erroneous opinion being formed regarding a case of suspected pancreatic disease are very appreciably diminished if the results of an examination of the urine and feces according to the methods I have described are considered in conjunction with the clinical evidence. It is yet too early to claim that they are pathognomonic, but it can be safely said that they are a most useful aid to diagnosis."

[These methods do not bear inherent evidence of scientific accuracy. They embrace many steps and the end result is capable of so much personal variation of interpretation, each step is so empirical, that it is difficult to understand how satisfactory results could be given. Other writers have not been able to verify the value of the methods. However, so little is known of the symptomatology of the pancreas that we must grope in the dark largely and much of rather blind reaching out is justified. —Ed.]

Modification of the Guaiac Test for Blood. Wile[1] suggests the following modification of the guiac test for blood.

(1) N. Y. Med. Jour. and Phil. Med. Jour., Oct. 7, 1905.

To equal parts of chloroform and turpentine tincture of guaiac is added drop by drop until a slight milkiness appears. To 2 c.c. of this mixture the suspected solution is added and the mixture is thoroughly shaken. In the presence of blood the mixture becomes blue in a few seconds, gradually deepens in color and then clears progressively until it disappears. Wile thinks the test is more delicate than the more usual method.

Mercury, Iron and Other Metallic Drugs in Relation to the Aloin and Guaiac Tests for Blood in the Feces. Guyot[1] found that after the administration of large doses of mercury the test was misleading. In his opinion this was due to the large amount of bile poured into the tract through the action of the mercury. Iron and the other drugs did not interfere with the test.

Lumbar Puncture in Diagnosis. Merzbacher[2] finds the following diagnostic uses for lumbar puncture in organic nervous diseases. In every case of paresis there is a marked lymphocytosis and in the majority of cases there is an increase in albumin. In tabes there is usually lymphocytosis without increase in albumin. Syphilis of the central nervous system causes lymphocytosis but not albumin increase in 80 per cent. of cases. Inflammatory meningitis, other than the chronic hyperplastic form, is accompanied by lymphocytosis. Psychoses show nothing.

Morphology and Reproduction of Spirochæte Pallida and a Rapid Method of Staining. Goldhorn[3] describes the following method: In 200 c.c. of water place 2 grams lith. carmine and add 2 grams of Merck's medicinal, Grubler's B X or Koch's rectified methylen blue. Heat in a rice boiler until a rich polychrome develops. Examine a few drops in a test tube against an artificial light every few minutes until a distinct red color is seen. Strain through cotton. To one-half of the solution add 5 per cent. acetic acid until a distinct red shows above the dye on a strip of litmus paper. To this add the other half of the dye. Now prepare a $\frac{1}{2}$ per cent. solution of French eosin; add this gradually to the blue, meanwhile stirring

(1) Gazzetta degli Ospedali, Milan, Vol. XXVII, No. 51.
(2) Rivista de Patologia Nervosa e Mentale, Vol. XI, May, 1906, quoted by Journal Amer. Med. Assoc., Oct. 20, 1906.
(3) Jour. Exp. Med., April, 1906, p. 45.

until a filtered sample is pale bluish with a slight fluorescence. Allow to stand one day and then filter. The precipitate is collected on a double filter paper and dried thoroughly at a temperature never exceeding 40° C. This preparation is dissolved in commercial wood alcohol, about 1 per cent. solution. Allow to stand for one day in an open vessel. Now filter. To use, drop enough dye on a film to cover it. Leave on 3 to 4 seconds. Pour off excess of dye. Slowly introduce the slide into clean water with the film side down. Leave in a standing position 4 to 5 seconds. Now shake in the water.

To make the films, the lesions were curetted so as to remove any pus and some surface epithelium. The curetting was continued until there was some oozing. Now an impression adhesion preparation was made.

Goldhorn found moist papules yielded the most consistent results. Chancres only yielded results from the edge of the sore. Roseola patches were sometimes productive, frequently not. Blood smears from the ear were seldom productive. Fresh specimens were best examined by allowing a hair to intervene between the cover and slide. This was better than a hanging drop. Movement was sluggish but otherwise the same as that of relapsing fever. The organism was by no means a uniform spiral. The number of turns and the closeness of the skin varied very much. Goldhorn was of the opinion that division was transverse.

Levaditi, quoted by Thiberger,[1] gives the following method of staining spirochæte in blocks of tissue: The pieces are fixed in 10 per cent. formalin, then in 95 per cent. alcohol. Wash for several minutes in distilled water. In 1.5 per cent. silver nitrate in distilled water for 3 days at 38° C. In a bath of 2 per cent. pyrogallic acid and 5 per cent. formalin at room temperature for 24 hours. Wash in distilled water. Dehydrate, imbed in paraffin. Stain with Giemsa.

Thiberger also quotes Bertarelli, Vulpino and Bovero as using the following method for microscopic sections: Thin sections are placed for 24 to 48 hours in 0.2 to 0.4 per cent. solution of silver nitrate in distilled water. They are

(1) Gazette des Hop., Jan. 27, 1906.

then plunged for 15 minutes in van Ermengen's bath (tanno-gallic acid and acetate of soda); wash in water; treat again with silver nitrate solution until the sections are a deep yellow tint; wash in water. Dehydrate, clear and mount in balsam.

[The Editor thinks it wise to call attention to the size of spirochæte. They are nearly as long as the diameter of a red blood corpuscle and they are about one-twentieth as broad. He has seen demonstrations of so-called spirochæte which were filaments of fibrin or strings of mucin and traversed much of an immersion oil field.]

Observations Upon the Phagocytic Power of the Blood of Supposedly Normal Human Beings. McFarland and L. Engle[1] have used the following method: In order to prevent coagulation, the blood is mixed with citrate of sodium, 1 per cent. in .85 per cent. salt solution. A tube 6 inches long with a caliber of 1 millimeter is taken. It is divided into compartments, each about 5 millimeters long. This tube is preceded with a rubber tube and mouthpiece. The citrate solution is drawn to the first mark and the blood next until the whole reaches the 2 mark. The mixture is blown into a receptacle and thoroughly mixed. To this is now added a standardized bacterial suspension in physiologic salt solution. The method of standardizing the solution will be next described. A tube 5 centimeters long is taken. This tube must be about 3 mm. in diameter and rather uniform. The bacterial suspension is drawn up to 5 and then the citrated blood until the whole stands at 10 cm. They are mixed in the tube or by blowing into a hollow sledge and then sucking back. After being thoroughly mixed and in the tube the ends are sealed. The tubes are then placed horizontally in an incubator at 37° C. for 30 minutes. The ends of the tube are broken and a small quantity of the mixture is blown on a cover glass and a film is made by using a second cover for smearing. The films are dried in the air and stained with Marino's stain. The bacteria are counted in 40 nuclear leucocytes and the results are averaged.

McFarland and L. Engle's Nephelometer. This instrument is for the purpose of standardizing turbidity in

(1) Medicine, April, 1906.

bacterial suspensions. Ten tubes of 1 per cent. solution sulphuric acid in distilled water were taken. To these were added 1, 2, 3, 4 to 10 per cent. of a 1 per cent. watery solution of barium chlorid. Ten test tubes were filled with about 3 c.c. of these solutions from 1 to 10. These test tubes

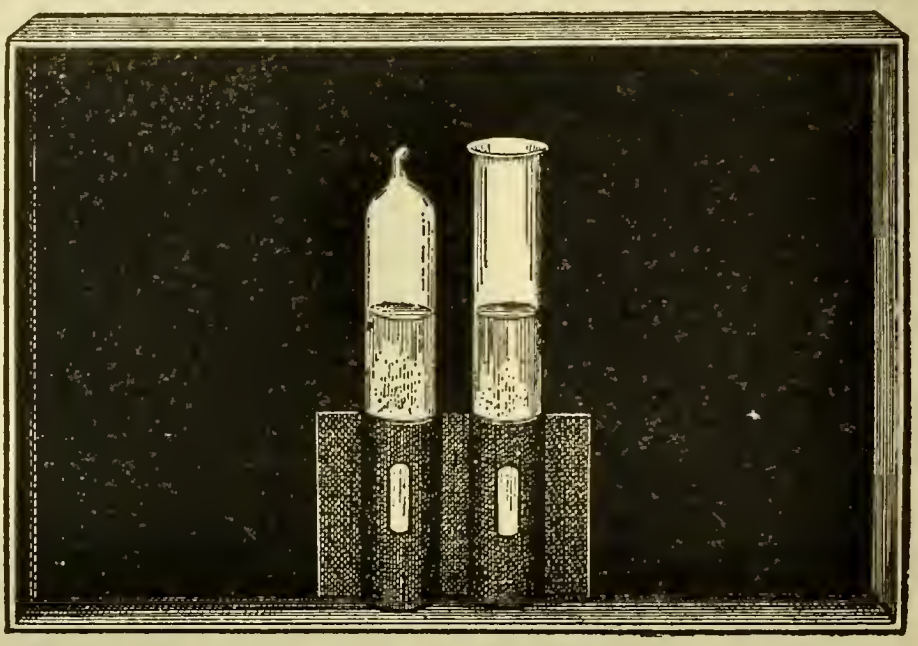


Fig. 2. Nephelometer.

were sealed and used as standards. Use was made of a small piece of cardboard with 2 slits about 2 inches long and $\frac{1}{4}$ inch wide. The tubes were viewed through these slits and with a bright sky or a white cloud as a background.

Marino's Stain.[1] The following two solutions are used:

No. 1.

Methylen blue	.5	grain
Azur II	.5	grain
Water	100.	grains

No. 2.

Carbonate of soda	.5	grain
Water	100.	grains

The two solutions are mixed and allowed to remain in the thermostat at 37° C. for 48 hours. At the end of this time a 0.2 per cent. solution cosin in water is added and the fluid is filtered. The preparation is dried in air and dis-

(1) Annales de l'Institut Pasteur, 1904, p. 761.

solved in pure methyl alcohol in proportion of 0.4 gram of precipitate to 22 c.c. alcohol.

To use, 4 small drops are put on cover and allowed to remain 3 minutes; then add 8 drops of 1 to 10,000 eosin solution for 2 minutes. Wash quickly in distilled water, dry, and mount in balsam.

Technique of the Tuberculo-Opsonic Test. Kinghorn and Twichell[1] give in detail the method of Wright and supplement it by certain modifications. Equal quantities of the patient's serum, an emulsion of tubercle bacilli and white blood corpuscles (washed in 0.5 per cent. sodium citrate in normal salt solution) are mixed in a capillary pipette and incubated at 37° C. for 20 minutes, after which blood films are made of the mixture and stained for tubercle bacilli. After counting the number of tubercle bacilli in a considerable number of polynuclear leucocytes the number per leucocyte is averaged. The opsonic index is calculated by comparing the average number per leucocyte with the average number in a given normal case. For example, assuming that the number averaged 3 and the number in a normal man averaged 2, then

3 :2 : :1 :X. X=1.5=opsonic index.

They made use of the following methods at Saranac.

Method of obtaining washed leucocytes: The finger is pricked and rendered turgid by winding a string around it. Five to ten large drops of blood are drawn into a 10 c.c. pipette with a short stem and a fine point and a fair-sized bulb. After each drop of blood a drop of 0.5 per cent. sodium citrate solution in 0.85 per cent. NaCl is drawn into the bulb and the mixture is well shaken. This mixture is then centrifuged in narrow tubes. The supernatant fluid is drawn off the corpuscles and 0.85 NaCl solution is added and the mixture is thoroughly shaken. Now this is centrifuged. The supernatant fluid is drawn off. Then the leucocyte layer is drawn off the red cell layer. The leucocyte layer is used for the test.

Method for obtaining uniform emulsions of tubercle bacilli (Baldwin): A quantity of tubercle bacilli from broth cultures is thoroughly washed and then dried in a desiccator; 150 grams are thoroughly ground in a mortar.

(1) American Journal Medical Sciences, Aug., 1906.

(b) This powder is placed in a flask with chloroform. Heat on a water bath with a return condenser. Filter the emulsion through hard filter paper. Wash the residue with hot chloroform. Dry in the air and then in a desiccator. Rub the residue in a mortar and repeat the extraction. (c) Suspend the residue in 185 c.c. cold chloroform and use as a stock; 0.3 c.c. of this is placed in a mortar, allowed to dry and then rubbed up with 1 c.c. of 0.1 per cent. NaCl.

Wright's method for a uniform tubercle emulsion: (1) Wash out the culture media with water filter, and finally washing with 15 per cent. solution NaCl; (2) rub up the washed tubercle bacilli in small hand mortar with 15 per cent. NaCl, continuing rubbing and adding salt solution until you have a paste which has the opalescence of thick ground glass; (3) centrifuge for a few moments to drive down the large clumps; (4) pipette off the supernatant emulsion, adding a little 15 per cent. salt solution; dilute the emulsion until a normal blood picks up about 2 to the leucocyte.

To use, take a piece of glass tubing one-quarter inch in diameter and four to five inches long. Heat one end and draw it out 7 to 8 inches. Fit this with a rubber nipple and mark a place about an inch and a half from the capillary end. Draw up the serum to the mark. Wipe the end. Draw in a little air. Draw up the leucocytes. Wipe the end of the tube. Draw in a little air. Draw up the bacterial emulsion. Blow the three into a receptacle; mix thoroughly. Draw back into the capillary tube. Seal carefully. Leave in the incubator at 37° C. for 20 minutes. Break the end of the tube and blow into a small saucer and mix thoroughly. Smear on slides, preferably slightly roughened. Stain as follows: Fix with wood alcohol. Heat in incubator at 37° C. for 10 minutes. Use analin fuchsin and decolorize with 0.5 per cent. HCl in 50 per cent. alcohol. Counterstain with Wright's stain. Dry and examine.

Method of Estimating the Opsonic Index. To the efforts at simplification of the technique of the opsonic index Simon and Lanear[1] contribute the following: About 0.5

(1) Johns Hopkins Hosp. Bulletin, Jan., 1906.

c.c. of blood is drawn up into a calibrated tube. It is transferred to a washing tube 5 c.c. in diameter, mixed with an excess of normal salt solution containing 0.1 per cent. oxalate of lime, and the whole centrifuged until the corpuscles have been well packed. The fluid is drawn off and replaced by normal salt, the mixture shaken up and centrifuged. This is repeated. The fluid is drawn off and the leucocyte layer is secured. Now 0.5 c.c. of the blood to be tested is taken and centrifuged at once, until the supernatant serum is clear. This serum is diluted with varying quantities of normal salt solutions and the different dilutions are properly labelled in small tubes. These tubes are inoculated with a suspension of bacteria until a moderate milky turbidity results. To them now is added some of the leucocytes and the mixture is incubated at 37° C. for 30 minutes. Smears are then prepared in the usual way. The point to note is which of the dilutions shows 90 per cent. of the leucocytes without bacteria. This is designated as the opsonic coefficient of extinction.

Diagnostic Value of the Leucocyte Formula in Pertussis. Churchill[1] quotes Karniski (Archiv f. Kind., 1903, p. 42) and Carstangen (Jahrbuch für Kind., 1900, Vol. LII, p. 215) as having established that the lymphocytes in the first year of life averaged 55 per cent. and the polynuclears 33 per cent. and that these proportions were gradually altered until in the ninth year the lymphocytes had fallen to 30 per cent. and the neutrophites had risen to 56 per cent. The total leucocyte count averages 13,500 in the first year. It falls to 9,000 in the second year and remains at this figure until the seventh year, when it falls to the adult numbers.

Studying 36 cases of whooping cough and reviewing the literature Churchill gathered the records of about 100 cases. He found that in cases of whooping cough in the first year of life the total leucocyte count averaged 32,000. In the second and third years 15,000. In the later years it was lower, but it never fell below 11,000. In the catarrhal stage of whooping cough there was a lymphocytosis in excess of the figures proper for that age in 93 per cent. of the cases. In no condition liable to be mis-

(1) Jour. Am. Med. Assoc., May 15, 1906.

taken for pertussis was lymphocytosis found. The great importance of these observations lies in this, that whooping cough is so difficult of diagnosis before the paroxysmal stage.

Ultra Violet Photo Micrography. Sabine[1] says that on account of the shorter wave length of the ultra violet rays a microscope using such rays alone should have twice the resolving power of an ordinary microscope of the same general power. An additional advantage is that all necessity for construction to prevent chromatic aberration having been removed, spherical aberration can be more advantageously met. Ernest and Wolbach, using such an apparatus, have been able to make plates with exceptional definition. They used fresh specimens in normal salt solution, Ringer's fluid, containing ½ to 1 per cent. agar, and lacrimal fluid.

Methylene Violet and Methylene Azure. No stains have added as much to the knowledge of recent years as have the various ingredients of the oxidized eosinated methylene blues. The true nature of the changes wrought in the blue by oxidation in an alkaline medium has proven elusive. Macheal[2] concludes that they are mixtures of methylene azure, methylene violet and methylene blue, and that some part of the staining is done by each.

In lieu of the rather uneven oxidation methods he offers the following formula for general blood staining:

Methylen violet (pure crystals).....0.08 g.
Methylen blue (med. pure).....0.16 g.
Eosin (water sol., yellowish, Gübler)....0.20 g.

Powder and mix thoroughly and dissolve in 100 c.c. of warm pure methyl alcohol. Cool to room temperature. Filter and dilute with 10 c.c. methyl alcohol. Use according to Leishman's method.

Or,—

Methylen violet (crude).....0.08 gr.
Methylen blue (med. pure).....0.08 gr.
Eosin (water sol., yellowish).....0.20 gr.

Dissolve in 100 c.c. methyl alcohol, filter and dilute as in the previous solution.

(1) Jour. Med. Research, April, 1906.
(2) Journal of Infectious Diseases, May, 1906.

To stain films so as to demonstrate the syphilitic spirillum substitute sodium bicarbonate (1 to 15,000) for the distilled water used to dilute in Leishman's method.

For staining malarial parasites and trypanosomes:

Methylen violet hydrochlorid	0.19 g.
Methylen blue (med. pure)	0.9 g.
Glycerin	50.0 c.c.
Aq., distilled	40.0 c.c.

Dissolve and add 10 c.c. of a 5 per cent. sodium carbonate solution. Allow to stand a few days and then use after the Nocht method, by adding a few drops to 2 to 10 c.c. of a 1 to 10,000 solution of eosin.

To stain spirochæte, use:

Methylen violet	0.2 g.
Methylen blue	0.8 g.
Glycerin	50.0 c.c.
Aq., distilled	40.0 c.c.

Dissolve and add 10 c.c. of a 5 per cent. solution of sodium carbonate.

The films should be fixed in pure methyl alcohol 3 to 5 minutes. Wash for a few minutes in 0.05 per cent. solution of sodium carbonate in water. Rinse well and then stain.

Also for malarial spirochæte, etc.:

Methylen azure hydrochlorid (pure)	0.5 g.
Methylen blue (med. pure)	0.5
Sodium carbonate	0.25
Glycerin	50.
Aq., distilled	50.

Dissolve. To use, add a few drops to a 1 to 5,000 eosin solution. Float the film on this for 10 to 15 minutes.

MacNeal, besides discussing the chemistry of the dyes and their probable relation to the effects produced in different cells, gives methods of production of the basic dyes, information that is not readily accessible in medical journals.

Staining of Fatty Acids and Soaps in Tissues. Benda's copper acetate process for demonstrating the presence of fatty acids in tissues has been modified recently by Fischer.[1] The chemistry of the combinations which take place when tissues are treated by this method is not fully determined, particularly with reference to oleic acid, but it is clear that the acid compounds are converted into insoluble copper soaps, which in the presence of hematoxylin form a varnish-like substance insoluble in weak acids.

Although the process is a very precise one, Oskar Klotz[2] recommends a modification of Fischer's method. By substituting a saturated solution of hematoxylin in 60 per cent. alcohol for Fischer's second solution, which is a saturated solution of hematoxylin in absolute alcohol, the writer claims that the neutral fats present in the degenerated tissues about calcified areas are not disturbed and are thus allowed to take the Sudan III or Scharlach R. stain.

The various steps of the process are as follows: 1. Fix the tissue and precipitate the fatty acids by treating the sections for one to twenty-four hours in the following solution: Chromatum 2½ grams, formalin 4 per cent., 100 c.c.—dissolve by boiling. While cooling add acetic acid 5 c.c. and then neutral copper acetate (powdered) 5 grains. 2. Thoroughly wash in water. 3. Cut on the freezing microtome. 4. Stain sections in a saturated solution of hematoxylin in 60 per cent. alcohol for six hours. 5. Wash sections in water and then treat with the following fluid (Weigert's decolorizing fluid) until the tissue becomes a light brown, while the sites of the fatty acid radical remain black:

Potassium ferricyanid.....	2.5 gm.
Borax	2.0 c.c.
Water, distilled	100.0 c.c.

The sections may be stained further with Sudan III or Scharlach R. whenever the relation of the fatty acids to the remaining fatty degeneration in the tissue is to be determined, and they are then mounted in Canada balsam.

This method of demonstrating neutral fats along with

(1) Centr. f. allgem. Pathol., 1904, vol. XV, p. 913.
(2) Jour. of Exp. Med., vol. VIII, No. 2, March 26, 1906.

the fatty acids in the tissues, either in the free state or in combination with bases in the form of soaps, is particularly useful in demonstrating the relation of the fatty acids and their salts to the fatty degeneration in all form of calcareous degeneration, such as calcified tumors, calcification of the arteries, and phleboliths.

Phagocytosis and Opsonin. By means of experiments giving comparable results Hektoen[1] found that the variable factor in a series of blood is the serum and not the leucocytes. Certain bacteria are taken up readily by leucocytes freed from sera, others are not taken up in the absence of sera. Just as there is variation in bacteria in reference to sera, there is variation in the same bacterium dependent upon the kind of serum which is used. The serum of a given animal varies much from time to time in its relation to the same bacterium. The substance in the serum which quickens the action of the leucocyte on the bacterium is an opsonin. Whether opsonin is a general defensive agent or whether there is a specific opsonin for each species of bacteria against which the body defends itself is a question. If it is a general body then it is subject to many modifications. It would seem that certain bacteria, under the influence of stimuli from the host increase in virulence, they become better able to defend themselves against phagocytosis in at least two ways, namely, by producing substances that are harmful to the phagocytes and by increased resistance to opsonification. Conversely we may think of the host as defending itself against certain infections by the production of opsonins and of antileucocidal substances. That a measure of the opsonic index may be of some diagnostic importance is possible. Many writers are of the opinion that it may help in determining prognosis and illumine the cause of certain phases of the clinical course of these cases.

Wright[2] has especially devoted himself to the bearing of the opsonic index on treatment. In tuberculosis the opsonic index is sometimes high and sometimes low. In his judgment the employment of tuberculin or other products of the tubercle bacillus for the purpose of producing im-

(1) Jour. Amer. Med. Assoc., May 12, 1906.
(2) Lancet, 1905, vol. II, p. 1,598.

munity during the course of tuberculosis is proper when the index is high. It is improper when it is low.

Somewhat similar conclusions relative to other diseases is tenable.

He proposes to make use of vaccines for curative and protective purposes, but the use of such agents must be based upon previous and contemporaneous determinations of the opsonic indices.

The Nature of Opsonins. Hektoen[1] thinks that bacterio-opsonins are distinct from the other antibodies, for the following reasons:

1. Heat may destroy the opsonic power of serum, leaving the lytic amboceptors intact.
2. Serum, normal as well as immune, may contain opsonin for a given organism, but not, so far as is yet known, the proper amboceptor for that organism.
3. A serum may contain opsonin for a bacterium, but no agglutinin, and the opsonin may persist after the bacteriolytic complement has been destroyed by heat.

He thinks that erythrocitic opsonins also are distinct substances for the following reasons:

1. Normal serum may contain hemolytic amboceptors, but not hemopsonins.
2. Immune sera may contain opsonic substances, but not amboceptors or agglutinins for the corpuscles in question.
3. By absorption methods the specific amboceptors in an immune serum may be separated from the specific opsonins.
4. The opsonic power of serum persists after the complement has been destroyed by heat.

Opsonic Index. McFarland and L. Engle, discussing opsonic index, are of the opinion that comparison can only be made with a man's own blood.

They conclude that Leishman's method as modified by Wright and Douglas and later by themselves is a practical clinical procedure and is simple enough for routine use, and accurate enough to be of some value in determining resistance to ordinary pus cocci and possibly also to tubercle bacilli.

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(1) Jour. Infect. Dis., May, 1906.

The Enzymes in Phagocytic Cells of Inflammatory Exudates. Opie[1] is of the opinion that the polynuclear, faintly granular leucocytes are derived from the bone marrow. Each secretes an enzyme which digests proteid more actively in an alkaline than in an acid medium. He terms this leuco-protease. The mononuclear leucocytes, like the liver, spleen, kidney and lymph glands, secrete an enzyme which digests proteid more actively in an acid medium. This he terms lympho-protease. This lympho-protease is not a pepsin, since it is not active in 0.2 per cent. HCl, and it is destroyed by precipitation and by drying with alcohol and ether. On the other hand, the leuco-protease acts much more slowly than loose trypsin.

Reque,[2] studying phagocytosis for diphtheria bacilli, concludes that this bacillus is very susceptible to phagocytosis. This is not materially affected by heating the bacilli. It has not been proven that diphtheria toxin favors phagocytosis. There is probably an increased formation of opsonin during convalescence from diphtheria.

Production of Active Immunity with the Split Products of the Colon Bacillus. V. C. Vaughan, Jr.,[3] demonstrates a possible immunity to colon bacillus which in addition throws some light on the principles governing active immunity. Making use of the method of Wheeler,[4] of splitting the cellular substance into two parts, he has found that the non-toxic portion has considerable immunizing power; the toxic portion has materially less. If colon bacilli are heated with a dilute solution of sodic hydrate in absolute alcohol, and this repeated three times, the residue will be very mildly toxic; the alcoholic extract will be violently so. This alcoholic extract when injected in increasing doses for some time produces a slight immunity to living colon bacilli. The nontoxic residue can be made use of to develop a much higher degree of immunity. The nature of the symptom-complex when this nontoxic portion is used, suggests that immunity is due to bacteriolysis. He postulates that it might even be fatal if the bacterial death and solution were rapid enough. The colon toxin is intra-

(1) Jour. Exp. Medicine, May, 1906.
(2) Journal Infec. Dis., May, 1906.
(3) Jour. Med. Research, Nov., 1905.
(4) Jour. Am. Med. Assoc., April 22, 1905.

cellular. Dead colon bacilli will split off poison just as will live ones, though the dose is not progressing, as when the bacteria are multiplying. The toxic portion is found in egg albumen and in peptone. This toxic portion is not entirely specific. The nontoxic portion is specific. Several points of great practical interest are developed by this series of observations taken in connection with the observations by Vaughan, Baxton, Wheeler and others. In the first place, possibly the nontoxic portions of other bacterial proteids can be made use of for the purpose of producing immunity. If, as Trudeau has shown, the soluble toxins of tubercle bacillus have less immunizing power than tubercle bacilli themselves, then possibly a similar technique may develop bodies of greater immunizing power. Secondly, cooking temperature may not render certain bacteria harmless, particularly those whose poison is but slightly soluble.

Nature of Phagocytes. Dudgeon and Ross[1] have found the great omentum of major consequence in infections of the peritoneum. When the peritoneal cavity was sterile after injections of various bacteria, bacteria could be recovered from omentum and phagocytic finely granular polynuclear cells were abundant. Even where sterile salt solution or sterile suspensions of salt were injected into the peritoneal cavity, and the general cavity remained sterile, the omentum showed *Staphylococcus albus.*

When virulent bacteria were injected into the peritoneal cavity, fluid was increased in 15 minutes and diminished in 24, except in the infections with colon bacillus and pyocyaneus. The predominant cell 15 minutes after injection was the small lymphocytic and the coarsely granular eosinophile. The coarsely granular eosinophile was an active phagocyte. This cell and the small lymphocyte did not agglutinate. After one hour the finely granular neutrophile was the predominating form. Occasionally microphages could be seen ingesting polynuclears and everything else.

In the blood there was an increase of the small polynuclear granules after fifteen minutes. In the bone marrow, for the first 24 hours the predominating cell is of the

(1) Journal Path. and Bact., March, 1906.

lymphoid, nongranular type. There were but few neutrophilic cells, as has been noted by Price Jones. The neutrophilic bone marrow observed by Muir after several days of infection was not observed in these less than twenty-four-hour cases. No phagocytosis was seen in the marrow. Nucleated red cells in the marrow were especially prominent in pneumococcus and streptococcus infections of the peritoneum.

The Great Omentum in Inflammation. Dudgeon and Ross[1] again emphasize the importance of examination of the omentum in autopsy work. Far from being passively rolled here and there by variations in peristaltic activity in different areas, it actively participates in inflammatory processes. *Staphylococcus albus* in their experience is normal in the omentum in many instances and can be grown from this viscus when cultures from elsewhere in the peritoneum are negative. Not only this, but in peritoneal infections omentum cells are the first and most active phagocytes.

The Origin of Antibodies, Precipitins and Agglutinins. Pfeiffer and Marx,[2] Wasserman,[3] and Levaditi[4] have shown through their researches that the bacteriolytic antibodies are produced by the leucocytes, the spleen, the marrow of bones and the lymph-glands. Kraus and Schiffman[5] conclude that the precipitins and agglutinins are formed in the blood. They are formed neither by the white cells nor by the red cells, but are probably produced by the endothelium of the blood-vessel wall. The amount of agglutinin in the blood is greater than in any organ and it may be recovered from the blood before it can be recovered from any organ. The same observations apply to precipitins. The writers have discovered that the precipitins are not continuously produced; in fact, their formation is a rather temporary expedient.

Experimental Anemias in the Rabbit. C. H. Bunting[6] has studied the effects of lymphotoxins and myelotoxins on the leucocytes of the blood and on the blood-forming

(1) Amer. Jour. Med. Sc., July, 1906.
(2) Zeitschr. f. Hyg., 1898.
(3) Berlin. klin. Woch., No. 4, 1898.
(4) Annales de l'Inst. Pasteur, 1904.
(5) Annales de l'Inst. Pasteur, March, 1906.
(6) Univ. of Penn. Med. Bull., 1903, vol. XVI, p. 200,

organs by using the immune sera obtained by immunizing geese to the various blood-producing organs and the blood of the rabbit. He also used ricin and saponin in his experiments, because they have a marked effect on the blood and blood-forming organs, but chiefly because they can be more easily standardized than the artificial sera; and the conclusions which he has drawn from this work are as follows:

Leucocytosis is the excessive reaction of the leucoblastic tissues to a leucopenia of the circulating blood. This leucopenia may be due to the withdrawal of leucocytes from the circulation or to their destruction within the circulation. The amphophile, eosinophile and basophile leucocytes are derived from the marrow. The lymphoid cells are chiefly derived from the lymph-glands and the spleen. The marrow, however, is a lymphoid tissue and contains typical lymphocytes. The lymphocyte is ameboid. Amphophile and eosinophile myelocytes may multiply by mytosis. Their number may also be increased by the development of specific granules in the protoplasm of large mononuclear elements with scant basophilic protoplasm, the least differentiated cell of the marrow and identical in appearance with the cells of the germinal centers of lymph-glands. Basophilic cells are formed by the development of basophilic granules in mononuclear cells. Multiplication by mytosis is not excluded by negative findings. Megaloblasts are a constituent of normal marrow and form the proliferating center of erythroblastic tissue.

Continuing his series of experiments on rabbits, Bunting[1] made further interesting observations on the structure of the cellular constituents of bone marrow and their reaction to various stimuli. Ricin and saponin in salt solution were the substances chiefly used for intravenous injections. The quantity generally used was 1-4 milligrams of saponin and 1/10-1 milligram of ricin in repeated doses.

From these experiments the writer concludes as follows: Nucleated red-cell crises in the circulating blood are the expression of injury to the bone marrow. The bone marrow reacts with nucleated cells only when the mature

(1) Jour. of Exp. Med., vol. VIII, No. 5, Oct. 12, 1906.

erythrocytes at the periphery of the erythrogenetic centers in it are destroyed by the action of a circulating toxin, or are depleted by excessive hemorrhage. In the first case the reaction is much more marked than in the second.

Following toxic injury to the marrow with destruction of the peripheral cells of the erythrogenetic groups there is established an atypical formation of erythrocytes resulting in pathologic forms, the most characteristic of which are the macrocytes. These appear to be directly derived from the megaloblasts without the orderly transition through the intermediate and normoblastic stages. This condition may represent an attempt at compensatory repair.

Following extensive injury to the marrow one may find the groups of blood-forming cells almost completely replaced by scar tissue. The spleen may then take on the hemopoietic function, the new cells being formed in the sinuses of the organ.

With subcutaneous injections of hemolytic toxins the absorption is so slow that the toxin is apparently saturated by cells in the circulation and does not reach the marrow in sufficient quantity to injure it. Under those conditions there is blood destruction, but no nucleated red-cell crises in the circulation, and the marrow picture is one of hyperplasia such as is seen after hemorrhage; i. e., the marrow of a secondary anemia.

Variation in the Peroxidase Activity of the Blood in Health and Disease. Kastle and Amoss[1] were stimulated by the researches of Jolles and Oppenheim[2] to study the variation in oxidizing activity of the blood in health and in several disease conditions. They found that when hydrogen peroxide is present normal blood at a dilution of 1 c.c. into 250 c.c. can oxidize 38.5 per cent. of phenolphthalin in one hour, whereas without it blood in a dilution of 1 c.c. in 100 c.c. oxidizes 4.6 per cent. in the same time. The maximum oxidation in the first instance is reached in one hour; in the last, in twenty-four. In normal blood without peroxide the color remains unchanged for 72 hours, in the blood of diseased persons the fading is more rapid. The blood of diseased persons behaves relatively like the

(1) Bulletin No. 31, Hygienic Laboratory.
(2) Virchow's Arch., 1905, pp. 180, 185 and 225, cited by Kastle and Amoss.

blood with peroxide; therefore the writers conclude that in the diseases studied there is a deficiency in oxidizing activity. There is also relation in peroxidase activity and amount of hemoglobin, though probably not all of the peroxidase activity resides in the hemoglobin.

The Toxicologic Constitution of Amanita Phalloides. This mushroom is the most poisonous of all the fungi and is responsible for most of the deaths from eating mushrooms. Ford[1] found two poisons present—phallin, or the hemolytic body of Kobert and amanito, a toxin first described in this article. Kobert's body is thermolabile and is destroyed by pepsin and pancreatin. Ford's body is thermostabile and is resistant to pepsin and pancreatin. They have different toxophore and haptophore groupings, as the antitoxin of one is not specific for the other. The Kobert body produces the subcutaneous edema, the hemoglobinuria, the pigmentation of the spleen and the blood laking. The Ford body produces hemorrhage, necrosis and fatty degeneration of the parenchymatous organs.

Rapid Diagnosis of Rabies. Frothingham[2] has studied the microscopic methods of diagnosis of rabies in a recent outbreak in Massachusetts. He is of the opinion that these methods are now so accurate that a biologic test is not required except it be for its psychologic effect. The Negri bodies he believes to be far more accurate than the van Gehuchten and Nelis changes in the ganglia. He expresses no opinion as to whether the Negri bodies are specific etiologic agents—probably protozoa—or specific degeneration products. These points for purposes of diagnosis are of secondary importance. The only important point is that the bodies are practically always present in rabies and are practically never present in other diseases. In his examinations he frequently found the bodies described by Volpino, and thought by the Italian to be the etiologic factor.

The Negri bodies were found in various parts of the central nervous system, but they were so much more frequent, regular and abundant in Ammon's horn that this

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(1) Jour. Exp. Med., April, 1906.
(2) Medical News, 1905, LXXXVII, p. 717, and Journal Inf. Dis., 1906, iii, p. 191.
(3) Jour. Med. Res., April, 1906.

is the stock site for examination selected. They are found in Purkinje's cells, sometimes in the granular layers—in fact they are liable to be found anywhere, but the preferred area is Ammon's horn. The bodies vary from 1 to 25 mikrons in size. Some of them have but little internal structure; others have a very definitely staining interior. The indefinite bodies are very apt to be mistaken for degenerated nuclei or for red cells. Therefore Frothingham thinks it best in diagnosis to disregard the smaller and less definite specimens.

The van Gehuchten changes consist in a proliferation of endothelial cells just within the capsule. Sometimes cells are found accumulating just outside the capsule. At the same time there is a ganglionic degeneration. The large nerve cells go to pieces and are replaced by endothelial cells. This change is found more pronounced and more frequently in rabies than are the Negri bodies, but unfortunately it is also found in diseases other than rabies. No special technique is required. Ordinary methods demonstrate the van Gehuchten changes well.

Frothingham concludes that the presence of Negri bodies means rabies as truly as the tubercle bacillus means tuberculosis, although inversely the absence of the Negri body does not necessarily mean the absence of rabies. If Negri bodies are not found, search the Gasserian ganglia for van Gehuchten changes. If the latter are found, do a biologic test—inoculate a rabbit. If they are not found, the case can be pronounced negative.

Negri Bodies in Hydrophobia. Davis,[1] examining five cases of human rabies, found both the Negri bodies and the Nelis-van Gehuchten reaction in all. He thinks the latter reaction of value in the diagnosis of hydrophobia, yet he does not think it has the same diagnostic significance as the Negri bodies. Of the Negri bodies he says that they are different from any morphologic entity, normal or pathologic, thus far known. They are specific, therefore, for this disease, and, whether degeneration product or protozoa, are important as diagnostic structures.

Epidemic Cerebrospinal Meningitis. Elser[2] finds that not

(1) Jour. Am. Med. Assoc., July, 1906.
(2) Jour. Med. Res., Nov., 1905.

all cases of epidemic cerebrospinal meningitis are due to Weichselbaum's diplococcus even in the same epidemic. While this organism is responsible for most of the cases, some are due to pneumococcus, some to streptococcus, and some to other organisms. The meningococcus is the only Gram negative coccus of importance except gonococcus and *Micrococcus catarrhalis.* Gonococcus in the nature of things would seldom be mistaken for meningococcus. *M. catarrhalis* was found in both forms described by Ghon and Pfeiffer,[1] the variety resembling meningococcus closely, and that, quite unlike *M. catarrhalis,* was very frequently found in the upper air passages in cases of meningitis. There may be relation between these organisms, for, amongst other reasons, the meningococcus was also frequently found in the air passages.

The best culture fluid for meningococcus was the Wertheim ascitic agar mixture proposed for gonococcus. The results on media made with ascitic fluids from different sources indicated possibly that the albumin percentage was of importance. Spinal fluid cultures were not always successful, and one negative result should not be accepted as final. Blood culture gave positive results in about 25 per cent. of the cases. In no case was blood culture of practical advantage in arriving at a diagnosis. Cultures from the urine, herpetic vesicle fluid and knee-joint fluid were negative. Examination of the brain showed nothing not previously described. There was an occasional small hemorrhagic area, an occasional thrombosis of the superior longitudinal sinus, and a rare thrombosis of neighboring sinuses. The middle ears show meningococci rather frequently. A semipurulent pericarditis without much roughening was quite frequently present. Elser remarks that this complicating lesion is probably frequently overlooked. The spleen was not often enlarged. The kidney, liver and heart showed rather inconspicuous parenchyma changes. The status lymphaticus was an etiologic factor and also appeared of prognostic importance in those fulminant cases terminating life in a few hours or days.

Disseminated Blastomycosis. Bassoe[2] reports the results of an autopsy on a case of generalized blastomycosis in

(1) Zeitschr. f. klin. Medizin, Vol. XLIV.
(2) Jour. Infect. Diseases, March, 1906.

which a consideration of the clinical history led him to conclude that the primary infection was in the lung. The patient had a cough, and the fungus was found in the sputum. Of the five cases of generalized blastomycosis reported from Chicago, four were deemed primary in the lung. Ophüls[1] says that blastomyces always originate in the skin. Coccidividal granuloma are liable to originate anywhere. In these cases, according to Ophüls, there is absence of budding in the tissue. Proliferation of the fungi is by endosporulation. In Bassoe's case there was budding within the tissue. Bassoe does not attempt to decide whether the coccidium body of Ophüls, the vidium body of Ricketts, and blastomyces are one and the same organism. He is certain that, whatever body it may be, it buds in the tissue. The lesions greatly resembled those of tuberculosis. They involved especially the lungs, the lumbar vertebra, and the adjacent tissues (psoas abscess), and some subcutaneous abscesses. As the result of prolonged suppuration there were extensive amyloid changes.

Generalized Blastomycosis. Christensen and Hektoen[2] report two cases of generalized blastomycosis. In one case the nature of the onset suggested an infection through the lungs and prompts the writers to suggest investigation of the possibility that the disease is air-borne. The lesions in the second case were in the deeper subcutaneous tissue and no part of entry was indicated with probability.

Bacteriology of Whooping Cough. Davis[3] has found a bacillus in the sputum of whooping cough. He thinks this bacillus probably the same as that described by Spengler[4] and Jochman and Krause.[5] It is identical, by ordinary means of examination, with the influenza bacillus of Pfeiffer. In fact, Davis is of the opinion that for the present we can do no better than to identify a hemophilicus group, a group growing only on media which contain hemoglobin, to which whooping cough and influenza belong, and leave methods of differentiating the members thereof to later study. The bacillus is short, small, faintly stain-

(1) Jour. Am. Med. Assoc., 1905, vol. 45, p. 129.
(2) Jour. Amer. Med. Assoc., July 28, 1906, Abst. Medicine, Oct., 1906.
(3) Journal Infect. Dis., March, 1906.
(4) Deutsche med. Woch., 1897, vol. 23, p. 830.
(5) Zeit. für Hyg., 1901, vol. 36, p. 193.

ing, does not take Gram. It probably stains best with a weak carbol fuchsin.

Actinomycosis or Lumpy Jaw. Salmon and Mohler,[1] revising the previous pamphlet by Salmon and Smith, conclude that actinomycosis seldom becomes generalized, and also that it is probably transmitted, both to man and animals, through grain. There is no evidence of direct transmission to man from eating meat. In view of these facts they think lumpy jaw cattle can be used for food with safety, provided the animal is in good flesh and the lesions have not become generalized.

Micrococcus Rheumaticus. Beattie[2] maintains that acute rheumatism or acute rheumatic fever is the result of bacterial infection is the opinion of most clinicians at the present day. Probably it is generally held that the infecting micro-organism is a streptococcus changed or attenuated in some fashion. It is the custom at Johns Hopkins hospital to make routine bacterial blood examinations in all cases of rheumatic fever, and Cole,[3] as the result of these observations, is of the opinion that the etiologic organism is a streptococcus. Beattie thinks that the freedom from endocardial vegetations, the suppurative arthritis, and other symptoms in Cole's cases prove that in each series, including the first, he was studying streptococci, and not *M. rheumaticus*. On the other hand, *M. rheumaticus* produces nonsuppurative arthritis and frequent endocardial vegetations in regions hitherto sound, in this showing marked contrast to streptococcus, which even in violent infections is not expected to affect a previously healthy endocardium. His examinations of the blood were negative, in this agreeing with the observations of Cole and Philipp,[4] opposing the conclusions of Poynton and Paine[5] and Beaton and Walker.[6] As to the relation of chronic to acute rheumatism, Beattie has but little to say. One or two of his experiments and one of Cole's lends some support to the idea that acute arthritis can eventuate in the proliferative and

(1) Circular No. 96, Bureau of Annual Industry.
(2) Jour. Med. Research, Jan., 1906.
(3) Journal Infect. Diseases, 1904, No. 4.
(4) Deutsches Archiv f. klin. Med., 1903, LXXVI, p. 150.
(5) Medico-Chir. Transactions, Lond., 1903.
(6) British Med. Journal, Jan. 31, 1903.

degenerative changes usually associated with the chronic arthritis.

Studies Upon Experimental Variola and Vaccinia in Monkeys. Councelman[1] is more than ever of the opinion that the cell inclusions of Guarnieri are the etiologic factors in smallpox. He is certain that the organism is living and does not conform to the type of other previously described organisms. The variations in structure are always in regular and progressive sequence, and present no marked similarity to degeneration processes or products. He discusses Ewing's theory that the bodies are specific degenerative products found only in smallpox, and due to the discharge of nuclear protoplasm into the cytoplasm. He cannot agree with this view, for negative reasons as well as the positive ones show that the organism is a living, developing body, having both an intranuclear and a cytoplasmic stage in variola, and a cytoplasmic stage only in varicella. Brinkerhoff and Tyzzer cite many authorities showing the susceptibility of different species of monkeys to smallpox. Amongst others they quote Anderson, Furlong and Charles Kingsley relative to spontaneous epidemics of smallpox amongst new world monkeys. It seems certain that new world monkeys are more susceptible than those of the old world.

Inoculating monkeys on the skin, they produced a typical vaccinia lesion. Inoculations on mucous membranes produced a disease only modified in so far as the local histology would be expected to modify the local lesions. Eye lesions were typical in corneal inoculation. Infection through the lungs was demonstrated. *Cytoryctes variolæ* were demonstrated in all local lesions. In variola inoculata in monkeys the lesions macroscopically and microscopically are identical with those in the human subject, as is the sequence of development. There are more polynuclear leucocytes in the serum of the pock than in the lesions of variola sera in man. This and some other differences are of minor importance. *Cytoryctes variolæ* in both the cytoplasmic and the intranuclear cycles is found in the lesions. They succeeded in inoculating through the corneæ, the mucous membranes, and through the deeper

(1) Jour. Med. Research, Jan., 1906.

respiratory tract. This last lends some support to the theory that in smallpox the primary inoculation is in the lungs, and that cytoryctes multiply there and cause a generalized infection; whether with or without a primary local pock in the lung has not been finally determined. Generally speaking, the laws of protective inoculation in monkeys are much the same as in the human subject. Vaccinia protects against variola more surely than variola protects against vaccinia. .

Cytoryctes were found in monkeys after the same general laws as in the human subject. Their occurrence in the endothelial cells suggested this as a means of spreading in the general exanthem of smallpox. They thought this occurrence and distribution of the inclusions is best explained by the hypothesis that they are living parasites.

Histology of the Skin Lesions in Varicella. Tyzzer[1] was not able to inoculate monkeys or rabbits with the fluid from chicken-pox lesions. They tried cutaneous scratches, vaccinations and washing of the intact and also the injured cornea. This of itself was sufficient to prove that chicken-pox and smallpox are not the same disease. The following methods of differentiating between variola and varicella are proposed by Tyzzer:

1. Examination of the clear fluid. In this in chicken-pox will be found very large multinuclear cells—balloon cells.

2. Excision of a typical lesion for microscopic examination. In variola one finds *Cytoryctes variolæ*. In varicella the pock appears different; there is ballooning degeneration; there are epithelial fibrils, fibrils of Herxheumer. There are cytoplasmic and intranuclear inclusions. These take an eosin stain. These eosin areas are the earliest things noted. The intranuclear forms stain red cloth eosin. The cytoplasmic forms stained purple with eosin hemotoxylon, and sometimes a central granula is formed. These lesions are generally first located in the corium. The corium lesions are always more pronounced than those of the epidermis. Tyzzer does not decide whether they are etiologic factors or more or less specific degeneration products.

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(1) Jour. Med. Research, April, 1906.

Field[1] does not think the bodies found in blister fluid in scarlet fever, noted by Mallory,[2] are protozoan bodies and of etiologic significance. He regards them as degeneration products. He has found them in measles and in other processes, and in such localities as lends support to the idea that they are degeneration products. He says that it is not possible to differentiate a degeneration product from a protozoan by a study of its morphology or its staining reaction.

Spirochæte Pallida in Syphilis. Alvarez.[3] *Spirochæte pallida* was announced by Schaudein and Hoffman to be the cause of syphilis. Its importance has been variously estimated by a large number of investigators. A reasonable estimate would be that the preponderance of evidence is very strongly in favor of the specificity of this organism. Some confusion has arisen from the general lack of information on the subject of spirilla. Beyond a doubt the study of spirilla in this and allied diseases, such as douraine, has added much to our knowledge of syphilis.

Spirochæte pallida has been found very frequently in the primary sore. It has also been found in the juice of the enlarged glands, in mucous patches, in the spleen, in the placenta. It is very difficult to find them in the peripheral blood even in cases of febrile syphilis.

Material to be examined unstained must be mixed immediately with normal salt solution, then mounted and the cover glass sealed. The organism is difficult to see in such preparations. Staining with Giemsa or Azar is the surest method of examination, and is easily done. Hastings stain diluted the same as for blood felons and used for 6 to 24 hours makes very pretty specimens. The specimens are first fixed in absolute methyl alcohol for 5 to 60 minutes and then left in dilute Giemsa for 1 to 15 hours.

Spirochæte was found in 7 out of 10 cases of undoubted syphilis. Tertiary ulcers were entirely negative.

Some of the most significant facts pointing to pallida being the cause of syphilis are:

1. Its practically constant presence in syphilitic lesions in their various stages.

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(1) Jour. Exper. Medicine, July, 1905.
(2) Journal Med. Research, 1905.
(3) Jour. Am. Med. Assoc., June 2, 1906.

2. Its constant absence in nonsyphilitic lesions.

In estimating the findings to the contrary we must bear in mind that most or nearly all of the investigators are untrained in the search for spirils.

3. Its presence in the organs of congenital syphilitics, and in the placenta.

4. The fact that only the pallida has been found in the deep tissues of syphilitics.

5. The numerical relation of the spirochæte to the virulence of the lesions.

6. The fact that *Spirochæte pallida* seems to be morphologically more distinct as a species than the other spiral organisms.

7. The fact that it seems to be highly differentiated as a parasite and soon disappears when removed from living tissues.

Spirochæte pallida has not yet been cultivated, and this is not likely to be easy of accomplishment on account of its marked parasitic tendency.

Experimental Syphilis in Monkeys. Thiburge[1] says that both chancroid and chancre can be inoculated in monkeys. In Macaque monkeys chancroids inoculated develop in 24 to 36 hours. It is at first a small, red pupule; soon there is a pustule, which breaks and leaves a small ulcer. This, if it is not irritated, heals in six to ten days. There is usually some local edema. The hard chancre has the same characteristics as to incubation period and physical characteristics as in man.

Syphilis of the Placenta. Wallich and Levaditi[2] report a case of syphilis of the placenta and fetus in which *Spirochæte pallida* were found in the blood of the intervillous spaces and decidua.

Spirochæte Pallida and Syphilis. Martzmowski[3] has found different forms of spirochæte rather abundantly distributed in the different tissues of the body in health and in various diseases. From the morphology of the organisms he thinks many of these can be differentiated from *Spirochæte pallida;* others cannot.

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(1) Gazette des Hopitaux, Jan. 16, 1906.
(2) Annales de Gyn. et d'Obstet., Feb., 1906.
(3) Med. Oborzenie, vol. LXV, p. 584, abstracted in Medicine, Oct., 1906.

Herman[1] is of the opinion that *Spirochæte pallida* is not the sole cause of syphilis. He suggests that blister fluid can be obtained in a few minutes by saturating some gauze with ammonia and binding it to the skin, covered by a watch crystal. In this blister fluid search can be made for *Spirochæte pallida.*

Intestinal Origin of Tuberculosis and the Mechanism of Tubercular Infection. Calmette and Guerin[2] conclude that animals of all ages easily contract tuberculosis through the digestive apparatus. The bacteria may traverse the intestinal wall without leaving any demonstrable lesion. In young animals the bacteria are arrested by the mesenteric glands, which become caseated and later calcareous. In adults the ganglia have not the same defensive capacity and in consequence the bacteria more frequently pass them and are picked up by the leucocytes which travel through the pulmonary arteries and locate in the lungs, as a rule.

Calmette and Guerin hold that primary pulmonary tuberculosis in the adult is most frequently of intestinal origin. They maintain that the intestinal route is the most efficacious of all modes of infection with tubercle bacilli.

Hereditary Syphilis. Levaditi[3] maintains that the *Spirochæte pallida* show a preference for the glandular epithelium. They have the capacity of penetrating the hepatic and renal epithelial cells and also those of the adrenals and the sweat glands.

Identity of Douraine and Syphilis. Mott[4] reports the findings in the spinal cord of an Arabian stallion dying of douraine. The lesions were located in the lumbo-sacral cord, and they very much resembled those of *Tabes dorsalis.* They were chronic interstitial in character and had originated in the perilymph vessel spaces in the cord. There was an infection with a trypanosome which involved the mucous tissue, then the submucosa. This then invaded the neighboring lymph vessels and by them was speedily carried to the nearby glands. The route of infection then is as follows: Inguinal glands, pelvic lymphatics, along

(1) N. Y. & Phil. Med. Jour., Dec. 9, 1905.
(2) Ann. de l'Inst. Pasteur, May, 1906.
(3) Ann. de l'Inst. Pasteur, Jan. 25, 1906.
(4) Brit. Med. Jour., Aug. 11, 1906, and Nature, July 5, 1906.

the lumbo-sacral nerves to the posterior spinal ganglia, where it sets up intense inflammation, resulting in destructive atrophy. The posterior cord areas are involved. There are pial and glial changes strongly suggestive of tabes. *Mal du coit* is due to a trypanosome. It clinically presents many points of kinship to syphilis. The apparent similarity of *Spirochæte pallida* to the trypanosome is another bond of kinship between them.

Two Cases of Relapsing Fever. The finding of so many parasites, both vegetal and animal in the blood stream, and the fairly well established etiologic relations of *Spirochæte pallida* and of the trypanosomes has stimulated study of all varieties of hematologic parasites. Carlisle[1] reports two cases of relapsing fever observed in New York city. The first was a seaman. Spirilla were demonstrated in his blood. These organisms drawn with the blood at the time of a paroxysm were successfully inoculated into monkeys. The bite of one of these monkeys was responsible for the second case. The article contains full reference to the history and geography of the subject.

The organisms found in these cases were inoculated in monkeys and white rats, and studied minutely by Norris, Poppenheimer and Fluornoy. They stained readily with Wright, Goldhorn, Jenner, Giemsa and other stains. They were difficult to find in fresh blood; frequently they could only be located through unexplained jerking of a red cell. Nothing characteristic was noted in the number of turns of the spiral or in the method of moving, or in the shape of the organism. These points are of importance, since they are points through which morphologic differentiation of *Spirochæte pallida* has been attempted.

All attempts at cultivation were unsuccessful, though in preparations of citrated human, and dead rats' blood, there was an increase in the number of parasites for a few days. The terminal filament of the spiral was drawn out like a flagellum. It stained with methylen blue. It was never multiple; all of the biology noted argues that these organisms are either bacteria or vegetal organisms in a hitherto undescribed class. Novy and Knapp,[2] study-

(1) Journal Infec. Dis., May, 1906.
(2) Journal Infec. Dis., May, 1906.

ing this organism of Carlisle, Norris and others, arrived at essentially the same conclusions, as follows:

1. The spirillum is a bacterium. Probably all the spirochæte belong to this same group. Probably there is a group of relapsing fevers embracing several different varieties.

2. In onset blood kept in vitro the organisms can be kept alive for 40 days. In decline blood the parasites speedily die, due probably to the presence of a germicidal agent.

3. Both active and passive immunity can be produced.

4. Agglutinins can be readily developed.

5. Both preventive and curative inoculations can be accomplished.

6. *Spirillum Obermeieri* can be made to pass through a Berkefeld filter.

Beriberi. Herzog[1] says that this disease clinically falls into three groups—acute, sub-acute and chronic. The acute pernicious forms resemble but little the less acute hydropic and dry atrophic varieties. He does not think the coccus described by Kokubo and Okata is the prime etiologic factor in this disease. He could not grow bacteria from the blood or organs with any degree of uniformity. Monkeys and other animals injected with culture fluids, previously inoculated with beriberi blood, remained healthy. Their blood developed no agglutinins or other specific antibodies that were determined. Nevertheless, Herzog is of the opinion that the disease is bacterial in origin. The bacterium gives rise to a toxin similar, he thinks, to that of diphtheria or tetanus, and which manifests a tendency to cumulative action. Primarily it is neither a nutritional disturbance nor a simple intoxication like lead, alcohol, arsenic or similar intoxications accompanied by multiple neuritis. It is an infectious disease. The pathology—the more important points—are as follows: Early post-mortem rigidity. Tendency to extravasations of blood and subcutaneous, mucous, and serous petechial hemorrhages; regional anasarca; hydropericardium, very frequently; hypertrophy and dilatation of all the component parts of the heart. The weight of this organ is increased from 15 to 25 per cent. above the

(1) Philippine Jour. Sc., September, 1906.

normal for the stature; there is fatty degeneration of the myocardium; toxemic degenerations of the liver and kidney; thickening of the mucous membrane of the gastro-intestinal tract.

Microscopically the peripheral nerves, especially those of the lower extremities, show marked changes—to the naked eye they appear normal. The changes, in Herzog's experience, are purely degenerative in character and limited to the myelin sheath and axis cylinder.

Trypanosomes of Tsetse Flies. Struck by the difficulty in reconciling certain observations of Schandinn, Koch, Gray and Tulloch, Novy[1] has studied the trypanosomes of Tsetse flies. He concludes that these are harmless forms, and not related to *Trypanosoma Gambiense* or *Brucei*. Mere morphologic study of various trypanosomes he thinks has led and is leading to false opinions. A given organism varies in size and shape according to differences in environment.

Malarial Fever of Cerebral Type. Chattergee[2] has studied three cases of malarial fever, cerebral type, all coming to autopsy. He found an abundance of pigmented bodies on the cerebral capillaries, as previously described by Councelman and Abbott, Bastionella, Bignami, Dock and others. These obstructed capillaries were found in both the gray and white substance.

In the center was a blood vessel plugged by agglutinated red cells, most of which contained malarial bodies. In addition there were multiple hemorrhagic areas, usually around the plugged vessels, and in these hemorrhagic areas all varieties of malarial organisms were found. The organisms were both pigmented and nonpigmented.

Studies on Yellow Fever. Marchoux and Simmond[3] state that yellow fever can become endemic only in those localities where *Stegomyia* is breeding all the time. In localities where no *Stegomyia* are found for several months in the year the fever can not be carried over from year to year, but must be reintroduced each season. The writers have noted that sometimes the mosquitoes show a capacity to transmit yellow fever from one generation of mos-

(1) Journal Infec. Dis., May, 1906.
(2) Jour. Path. and Bact., Aug., 1905.
(3) Ann. de l'Inst. Pasteur, May 25, 1906.

quitoes to another; that is, occasionally an infected female will lay a crop of eggs developing into mosquitoes capable of transmitting yellow fever without themselves being independently infected. Such transmitted infection, however, is not the rule and is never carried over more than one generation. This hereditary transmission only occurs through eggs laid twelve or more days after the infection has taken place and the young mosquitoes can not transmit the disease until they are more than fourteen days old. The writers have observed that the female never transmits the disease during the day time. People can suffer mosquitoes to bite them during the day time with impunity.

An interesting observation was that the female *Stegomyia* did not die after partaking of blood; she may live twenty to thirty days and lay as many as seven sets of eggs. In the interval she may bite a variable number of men. If *Stegomyia* died within eight days after sucking blood, as do the *Culisidæ,* then yellow fever would be unknown in the human race, twelve days in the body of the mosquito being needed to complete the sexual cycle and make the parasite ready for the asexual cycle in the human host.

The writers found that mosquitoes fed on vomit from cases of yellow fever had no capacity to infect. The only method of transmission of the disease to mosquitoes was through live blood drawn directly from the capillaries of a patient sick of yellow fever less than four days.

The pathology is essentially one of generalized steotosis. This change is found in all organs, but in some it is more marked than in others. It affects especially the liver and the endothelium of the blood-vessels. The epithelium of the skin glands is relatively spared, as is that of the intestinal tract. [This capacity of the mosquito to transmit the parasite through the egg to the young is without parallel in parasitology, assuming, of course, that the writers are correct in their observation. That spontaneous generation, or, rather, that reproduction without sexual stimulus, can be carried on for a very few generations is recognized for insects as high in the scale as bees. Very much lower organisms, for instance the malarial parasite, can reproduce for a large number of cycles without sexual stimulus. In each group, however, the sexual stimulus

must be reproduced after a while or the generations of beings come to an end. The explanation is, of course, that in short-lived individuals some of the male exciting substance is actually carried along from being to being in the different generations, but the carrying along of pathogenic organisms—parasites—in this manner, is quite a different matter.—ED.]

The Blood in Yellow Fever. Early writers believed that the histologic elements of the blood were completely destroyed in yellow fever and its coagulability equally impaired. L. H. Marks,[1] superintendent of the Emergency (Yellow Fever) Hospital, New Orleans, maintains that the coagulability of the blood of patients with yellow fever is normal. He has frequently noted that blood drawn from the median vein of a yellow fever patient coagulated before it could be forced out of the aspirator into a receptacle held ready to receive it; the time was not more than from three to five minutes. It was frequently necessary to add a solution of potassium oxalate to the blood before performing certain filtration experiments so as to overcome its readiness to coagulate.

The normal coagulability of the blood in yellow fever has also been ascertained in a series of actual experiments in which the results have been recorded by means of Wright's coagulometer.

The writer mentions that in over twenty thousand examinations of fresh and stained preparations of blood of yellow fever patients made by the various workers at the Emergency Hospital at New Orleans during the epidemic of 1905 not one specimen showed the slightest evidence whatsoever of corpuscular degeneration.

Bedbugs and Human Diseases. Girault[2] has found that the human bedbug will live, thrive and propagate when feeding on the blood of mice, bats, and probably other animals living in the habitations of men. The fowl bug also would suck the blood of other animals. The author thinks it probable that some human diseases can be transmitted by bedbugs.

Spotted Fever. Ricketts[3] was unable to verify the find-

(1) Jour. of Med. Sc., vol. CXXXII, No. 5, Nov., 1906.
(2) Journ. Amer. Med. Assoc., July 14, 1906.
(3) Jour. Am. Med. Assoc., July 7, 1906.

ing, by Wilson and Chowning, of an animal parasite in the blood. No staining demonstrated anything which he could interpret as of etiologic significance. Aerobic and anaerobic cultures on media of several kinds were also negative. Injections of blood were made into monkeys and guinea-pigs, resulting in a fever which in the severer cases gave skin lesions similar to those of spotted fever. Blood from the animals dying from the induced disease was injected into a new lot of guinea-pigs and monkeys. In this way the disease was transmitted for several generations. There was a gradual subsidence of virulence. Ricketts endeavored to keep the virus potent by alternating the host from monkeys to guinea-pigs, and vice versa. He is of the opinion that the transmitted disease was not an intoxication but was an infection. This was proven, in his judgment, by the transmission of the disease through a series of animals.

In a still later paper Ricketts[1] announces that the plan of alternating monkeys and guinea-pigs as hosts for spotted fever has proven successful, and that he has now kept the disease going for several months. The inoculation is by injection. This demonstrates that whether or not ticks serve a purpose in spreading the disease, their function is not essential. They are not obligatory hosts of any cycle or portion of a cycle.

A laboratory life history of a Montana tick was as follows: Females were placed in jars on May 20. June 21 they were laying eggs. June 28 six-legged larvæ were hatching. July 13 these attached themselves to guinea pigs. By August 1 they were dropping off. August 5 they were moulting eight-legged nymphs. August 12 to 15 they attached themselves to guinea-pigs. August 30 they were full grown adults, ready for another cycle.

King,[2] working with the same material, transmitted the disease to guinea-pigs through the bite of ticks. This was independently observed also by Ricketts.[3]

Mayo[4] says that the disease is common in the spring in Montana, Idaho and Wyoming, amongst bridge builders, carpenters and engineers, and other men whose work fre-

(1) Jour. Am. Med. Assoc., Oct. 6, 1906.
(2) Public Health Reports, July 27, 1906.
(3) Jour. Am. Med. Assoc., Aug. 4, 1906.
(4) Jour. Am. Med. Assoc., July 7, 1906.

quently causes them to sleep on the ground. He quotes a personally expressed opinion of Welch that the supposed organisms in the blood are degeneration products.

Mooser[1] reports seven cases amongst sheep herders, who gave histories of recent bites by ticks.

Amebiasis. Wooley and Musgrave[2] say that while the ameba lesions are usually characteristic, they are not always so. Certain cases cannot be told from the naked eye appearances from tubercular or other ulcerative lesions. In about 87 per cent. of cases the entire colon is involved. Probably in untreated cases the percentage is higher still. The process probably never invades the small intestine except for a few lesions at the lower end of the ilium. The ulcers are markedly undetermined. Ameba traverse the *muscularis mucosæ* often while that membrane is still intact. They also seem to have a disposition to go into the blood-vessels by ameboid movement. The disease is subacute or chronic. In the lesions few leucocytes are seen. The cells are lymphocytes, fibroblasts, plasma cells, eosinophiles, and sometimes mast cells. The authors found no evidence that bacteria limited the work of ameba or assisted them in the destructive processes. In fact, many ameba were loaded with bacteria.

The lesion of the disease was essentially a necrobiosis. Complete healing may occur, or there may persist a chronic atrophic enteritis or chronic catarrh known as sprue or psilosis.

Uncinariasis in Mississippi. It will be remembered that Stiles' tour of the South in search of hook worm stopped at Florida. Subsequently Kirby Smith found the parasite in Mississippi, and Stiles, in 1904, while on a short visit to Jackson, found a few cases. In the intervening years scattered cases have been reported. The topography as well as the latitude of the state suggested to Bass[3] that hook worm probably exercised much influence on health and economies of the state. By personal investigation and by joint study with the physicians of the state he found the disease widespread. There was a good deal in Delta counties, such as Washington and Bolivar, and some

(1) Jour. Am. Med. Assoc., Sept. 1, 1906.
(2) Journal Am. Med. Assoc., Nov., 1905.
(3) Jour. Am. Med. Assoc., July 21, 1906.

in prairie counties, such as Monroe—it was out in sandy counties that it was more widely spread. Dr. Bass estimates that it affects 50 per cent. of the population in counties such as Marion. He recommends the following improvement in the technique of examination of feces for eggs: A small piece of feces is shaken up with salt solution, nine-tenths saturated, and allowed to stand 5 to 30 minutes. The feces settles to the bottom and the eggs float on the surface, and a drop of the surface water will show a maximum number.

Statistical Study of the Prevalence of Intestinal Worms in Man. Stiles and Gurrison[1] examined 3,457 inhabitants of institutions, principally insane asylums, and found 349, or 10.1 per cent., infected with some intestinal parasite. The presence of two or more species together was found 36 times. The relative frequency of the different parasites was: *Trichures trichiuria,* 266; oxyuris, 45; hookworms, 36; ascaris, 17; *Hymenolepis nana,* 12; *Strongyloides,* 8; *Tenia saginata,* 2. The authors think probably oxyuris is more frequently present than these figures show, since routine examination of feces frequently fails to demonstrate oxyuris when it is present. Particular attention is directed to the 12 cases of short tapeworm Hymenolepis, and this is contrasted with the 2 cases of *Tenia saginata.* Only about 28 cases of infection with the short tapeworm have been reported in the United States. (See Ransom, Bulletin 18, Public Health Service.) As to the immunity of the colored race to uncinaria these writers suggest that the immunity is against the effects of hookworm rather than to hookworm itself. The probability is that negroes are infected to about the same degree as whites, but they are not rendered profoundly anemic thereby as are the whites.

C. W. Stiles[2] describes *Hymenolepis nana,* the dwarf tapeworm, substantially as follows: One hundred to 250 segments, usually broader than long. Total length 5 to 45 m.m. Head, 130 to 480 in diameter. Rostellum well developed. Single row of 20 to 30 hooklets. Globular suckers. Eggs oval or globular, with two distinct membranes. Outer membrane, 30 to 60 microns in diameter.

(1) Hygienic Laboratory Bulletin, No. 28.
(2) Bulletin No. 25, Hygienic Laboratory.

Inner membrane, 16 to 30 microns in diameter, presenting at each pole a teat-like projection with filamentous appendages. Habitat—Small intestine of rats and men. Development—The embryo is swallowed, then hatched, and gets into an intestinal villus, where it becomes encysted, and in turn falls into the lumen of the intestine and becomes an adult.

MALIGNANT DISEASE.

J. D. Bryant[1] maintains that cancer is not a disease of locality. Geographical considerations are of minor importance. Zoologically it seems equally widespread. It seems to affect all vertebrates from the lowest to the highest. The highest forms of life pay heavier tribute to this disease than do the lower. Man suffers more than all other animals combined. No organ or tissue of the human body is entirely free from its visitation.

Harvey regarded cancer as a parasite on the body, living an independent existence at the expense of the latter. Hunter seems to have been the first to recognize the influence of traumatism as a causative factor of cancer, aided by the consequent exudation of coagulable lymph into the interstitial tissues. The two extremes of opinion at present as to the cause of cancer are the following: First, that cancer is due to a micro-organism; second, that cancer represents a morbid proliferation of certain normal cellular elements as a result of diminished inhibitory action. The relative extent of invasion by cancer of the accessible, of the inaccessible, and of the intermediate parts of the human body affords an interesting study.

Those superficial parts of the body falling readily under the scrutiny of the unaided eye and the touch of the physician are manifestly the seat of accessible cancer. Those deep and internal parts of the body, conveniently placed beyond the limits of unaided vision or mere touch, are the sites allotted to inaccessible cancer. Those portions of the body within the reach of the finger and aided inspection are, for the most part, the sites of intermediate cancer.

The development of cancer of the parts included in each of the foregoing divisions of the body is compara-

(1) Jour. Am. Med. Assoc., June 9, 1906.

tively much less manifest in individuals under 25 years of age than in those above that period, standing in this respect nearly as 1 to 70. The male sex suffers nearly 22 per cent. greater infliction from malignant disease than the female, during this time, which can be accounted for in part, at least, by the greater strenuousness of the male and the effect of the exposures incident thereto. The probable reasons for the greater infliction of the sexes under, than over, 25 years of age, seem to have been considered sufficiently already.

The comparative difference between the frequency of occurrence of accessible and inaccessible cancer in both sexes, under and over 25 years of age, is astonishing, even when proper deductions are made for the greater uncertainty of diagnosis in the latter kind. Inaccessible cancer in males of 25 years and under is 80 per cent. more frequent than the accessible kind. Inaccessible cancer in females of 25 years and under is nearly twice as frequent as accessible cancer. Inaccessible cancer in males above 25 years of age is three times more frequent than the accessible variety. Inaccessible cancer in females over 25 years of age is about $2\frac{1}{4}$ times more common than accessible cancer. Inaccessible cancer in males regardless of age is approximately three times more frequent than the accessible variety. Inaccessible cancer in females, irrespective of age, is 2 1/5 times more common than the accessible. Inaccessible cancer is, without regard to age or sex, a trifle more than $2\frac{1}{2}$ times more common than cancer accessibly located.

While it is now, and has long been conceded, that external influences, traumatic and otherwise, contribute to the frequency of accessible cancer in a greater or less degree, it is also self-evident that other and more potent agencies than these must be invoked to account not only for the occurrence of inaccessible cancer but also for its great preponderance over those accessibly located at all periods of life, more especially the dominant one, that above 25 years of age. The increase in cancer visitation, in connection with advancing years, has long been a matter of common knowledge. But that the location of cancer, at all times of life and especially in adult life, should be of inaccessible, rather than of

accessible nature, is more than remarkable, it is even startling, suggesting in no common tone the idea that, directly or indirectly, subtler influences than external traumatism or infecting agents can exercise are active in the development and spread of cancer. Perhaps it may be consistently said that the traumatisms thoughtlessly inflicted on the gastrointestinal tract by the yielding to the temptations and pleasures of life—while less emphatic than those directed to the external surface—are none the less potent for evil because of the fact that their frequent and prolonged action may increase correspondingly an ill effect. However this may be, it appears quite reasonable to some that cancer organisms coming somewhere from without implant themselves in the tissues and develop there, notwithstanding the inhibitory effect of cooking, the power of digestion, the opposition of phagocytosis, and the fickle element of chance.

It is fitting now to remark that there appears to be no good reason to believe that the food of a people influences their relation to malignant disease in an appreciable degree.

Intermediate cancer in both sexes under 25 years of age is about half as frequent as is accessible cancer in both at the same period, possibly showing thus early in life the benign effect of protection of the intermediate parts from ordinary external influences. In the male after 25 years of age intermediate cancer shows a comparative decrease in rate from that of the accessible form of about 32 per cent., suggesting that the evil effect of external influences are superior in potency or greater in number in the male than are those causing intermediate cancer. In the female during this period (after 25 years) the rate of accessible cancer exceeds that in the male by about 37 per cent. The intermediate variety, however, at this time in the female exceeds the accessible form by more than 48 per cent., showing the rapid increase in the intermediate variety due to pelvic disease, which cannot be attributed in any practical degree to infection, but mainly to the traumatisms of maternity and the age limit of certain nearby tissues. It should be stated in this connection that the liability in both sexes to cancer of the gastrointestinal tract, gradually and quite uniformly diminishes from the stomach down-

ward toward the external opening, but not including it. This fact seems to justify the thought already stated regarding the possibility of the effect of dietary traumatism on the stomach and the upper intestinal tract.

The age limit of the tissues of the stomach in health conforms to the nutritive requirements of the life to which they are all important, consequently this feature of the causation of cancer, which so freely contributes to the total of this disease in the mammary gland and the uterus, can play no part in the causation of cancer of the stomach, making it, therefore, the more apparent that alimentary traumatisms and dietary abuses are dominant influences in the causation of gastric cancer. Another fact which seems to confirm this position is that cancer in the male in the alimentary canal is quite seven times as common as in the female, notwithstanding the further fact of the general tendency of females to suffer from cancer of the alimentary canal at an earlier age than males. Surely, if cancer of the stomach were dependent in an appreciable degree on parasitic infection of alimentary substances this great difference in the relative proportions of infliction of the sexes should not exist. Finally, in males 80 per cent. of all cancer affects the alimentary canal. In females 80 per cent. of all cancer affects the reproductive tract, including therewith the breast.

Carcinoma in Early Life. Grule.[1] Carcinoma of the rectum occurs in children even under 10 years of age, which may perhaps be explained by the frequency of adenoid growths in children. Gelatinous cancer is almost exclusively found in young persons. From 2 to 3 per cent. of all rectal cancers occur in persons between 20 and 30 years of age. Busk, in 1846, reported a medullary sarcoma of the rectum in a boy 16 years old, but by later writers this has been accepted as a carcinoma.

Roentgen Rays and Growing Tissue. Foersterling[2] describes experimental effect of x-rays on young animals and growing plants. When a single application of the rays is made a marked arrest in the growth of the exposed tissues of the body was demonstrated. When the animals are older the effect is not as noticeable as in the young. A

(1) Surgery, Gyn. and Obst., June, 1906.
(2) Central. f. Chir., No. 19, 1906.

less severe application also is more detrimental to very young animals. Great precaution is urged in the treatment of children by x-ray. The writer was not able to decide as to the least amount of exposure that would affect the tissues.

Glioma of Brain. Bassoe,[1] in reporting three cases of glioma of the brain, emphasizes the following points: The amount of fiber formation was much less in the two cases, 4 to 6 weeks in duration, than in the case which lasted three weeks or more. The latter greatly resembled sarcoma, except for some perivascular cell arrangement and for a small number of fine glia fibers. In the more chronic case the fibers were abundant, coarse and easily stained.

Tumors of the Carotid Gland. Keen and Funke[2] report another of those comparatively benign tumors usually called peritheliomas. They spring from the carotid gland at the bifurcation of the artery of the same name and they usually appear at the anterior border of the sterno-mastoid muscle at about its middle. The tumors are alveolar in arrangement. Each alveolus contains about 50 cells closely resembling endothelial cells. The walls of the alveoli contain fairly definite blood capillaries. These tumors have slight tendency to invade the carotid sheath. They seldom form metastases.

Loeb[3] has added many observations to the circumstances governing transmissions of tumors. He divides the variable factors determining the rate of tumor growth into two groups: (1) Condition present in the tissues, lymph and blood of the animal; (2) the inherent growth energy of the tumor cells.

Under the first group Jensen, Herzog, Michaelis, Gaylord, Sticker and Loeb have demonstrated such facts as these: Transplanted tumors will not grow in animals of a different species. After repeated inoculations some immunity was secured. Aside from species immunity there is individual immunity in some cases. There is some evidence of geographic immunity. Individual predisposition becomes of greater importance as the inherent

(1) Trans. Chicago Path. Society, April 9, 1906.
(2) Jour. Am. Med. Assoc., Aug. 18, 1906.
(3) American Med., Aug. 12, 1905.

growing energy of the tumor declines. Under the second head, namely, the growing energy of the tumor cells themselves, Loeb offers the following provisional laws: The energy of tumor growth can be increased directly by the removal of the tension of the surrounding capsule. It is possible to cause an experimental increase and decrease in the energy of tumor growth. These variations are due to causes acting directly on the cells. Such action may be cumulative. The transplanted cells may grow more rapidly than in the original location, and this is due probably to causes resident in the cells themselves. The cells left behind may also take on renewed growing energy.

Infectious Lymphosarcoma of Dogs. The question of the etiology of tumors is still attracting much attention at the hands of scientists. The number of successful inoculations of tumors increases. There are many reports on Jensen's tumors in mice. Many men have succeeded in inoculating tumors obtained from one animal into an animal of the same species, but efforts at inoculating tumors of one animal to an animal of a definitely different species have not succeeded. This is an argument in favor of the biologic basis of tumors and against the parasitic theory, and this, in spite of the work of Gaylord, is unquestionably the trend of the times. Beete and Ewing[1] suggest that infectious lymphosarcoma in dogs is a splendid tumor for the study of etiology in tumor formation. It is frequently found and easily inoculated. It exists in large animals which are easily controlled. It is found on the genitalia, forms metastases, and is infectious on coitus. Histologically the tumors are composed of large polygonal cells with pale staining protoplasm and single nuclei with prominent nucleoli. The cells are arranged in cords separated by delicate tubercular bands. The tumors are soft, grayish white, and a mucin substance can be squeezed from them. If one be rubbed on the mucous membrane of the genitalia there is a slight inflammation, which subsides in a few days and in a few weeks the tumor begins to grow. Careful examination by Beebe and Ewing shows that the tumor springs from implanted cells and that the tumor cells in the new host are the

(1) Journal. Med. Research, Sept., 1906.

product of multiplication of cells of the old host. This is held by Bashford, Murray and Cramer[1] to be the crucial distinguishing point between an infectious granuloma and a true tumor. They concluded that when the cells of an infectious lymphocarcinoma were implanted in a new host the old cells died and the tumor was due to proliferation of the cells of the new animal. As before said, Beebe and Ewing are of the opposite opinion. In these tumors no one has found spirals. Beebe and Ewing think them true tumors, with unusual capacity for independent existence and infectivity unapproached by any other true tumor. Infectivity is seen in such undoubted tumors as carcinoma a deux. That the tumors spontaneously recover is also no negative argument, as the same thing occasionally occurs in cancers.

Infectious Venereal Tumors in Dogs. Reitman and Amadon report ten cases of venereal tumors in dogs. These tumors are very contagious and are capable of being communicated from dog to bitch and vice versa during copulation.

Macroscopically the venereal tumor has a cauliflower appearance similar to the soft papilloma. They somewhat resemble the venereal wart in man. They begin as small yellowish white raised patches about the size of a mustard seed, growing into clusters of friable masses which bleed readily when touched. These tumors grow to considerable size, and when removed by operation, reoccur. There is a slight tendency to metastasis in the adjacent organs.

Microscopically, on superficial examination, these tumors appear to be small, round-celled sarcomas. The cells which make up the tumor mass are principally small, round cells, having a vesicular nucleus. Mitosis can be seen. They invade the surrounding tissues similar to the sarcoma cell. A thin covering of stratified squamous epithelium surrounds the tumor masses. In some of these tumors embryonal connective tissue cells in every stage of growth are present. Two of these tumors presented a characteristic endotheliomatous appearance. Various attempts were made to find the etiologic factor. A small yeast-like body was found in each of the tumors,

(1) Veterinary Journal, 1905, n. s., VII, p. 298.

but they were unable to isolate it. Stains for the *Spirochæte pallida* were negative.

Glycogen in Tumors. Odier[1] states that all growing tumors are charged with glycogen. The disappearance of glycogen from tumors subsequent to erysipelas caused Odier to investigate the possibilities along this line. Since temperature seemed to exercise some influence he has tried injections of tetanus bacillus, which produces so much hyperpyrexia. He has arrested the growth of young animals by injecting tetanus bacilli. He does not state whether he has tried this method of arresting the growth of tumors. In certain diseases the blood contains an excess of glycogen, *e. g.,* rheumatism and malignant growths. He says there is great difference between spontaneous development of tumors and inoculation therewith. He says that underlying the growth of tumors is a glycogen diathesis which must be reckoned with. If not, recurrence will occur, even after the best of operative procedures.

In examination of 4 cases of sarcoma, 19 carcinoma, 2 papilloma and 1 adenoma the amount of glycogen in the blood was always greater some hours after placing in the oven than when first placed there.

He treated the cases by injecting solutions of glycogen and pancreatic ferment. In the first 24 hours the tumor increased in size and the temperature rose several degrees. This elevation of temperature did not occur in the healthy animals. After these daily injections had caused the tumor to appreciably diminish in size and rest quiet the glycogen was reduced from 4 to 6 gr. per 1,000 to .03 per 1,000.

Askanazy in the discussion called attention to the following facts: Ordinary carcinomata of the mammary gland and stomach contain no glycogen. When a primary tumor is rich in glycogen a metastatic growth from the same stock may not show glycogen. There is not a parallelism between glycogen content and proliferative energy. It is necessary to remember that glycogen is normally most abundant in the tissues from which tumors are most liable to grow.

Malignant Disease of Thyroid. Müller and Speese.[2] The

(1) La Presse Medicale, June 30, 1906.
(2) Univ. of Penn. Medical Bulletin, June, 1906.

literature shows that there has been previous goiter in about 55 per cent. of the cases. About 60 per cent. of the cases are in women. Both sarcoma and carcinoma show a preference for the carcinoma decades. The capsule prevents spreading for a long time. The trachea perforates in 8 per cent. of the cases and the esophagus in 4 per cent. Metastasis occurs in 85 per cent. of the completely recorded cases. Of these 50 per cent. of the carcinomas metastasized by way of the blood vessels and 20 per cent. of the sarcomas by way of the lymphatics. In 238 cases collected by Ehrhardt the more frequent metastases were:

	Carcinoma.	Sarcoma.
Bones	49.29 per cent.	24.18 per cent.
Lung	72.42 " "	65.48 " "
Liver	5. " "	16. " "
Kidney	14. " "	10. " "
Brain	7. " "	5. " "
Pleura	12. " "	6. " "

In 65 cases of bone metastasis Ehrhardt found: Skull, 35; sup. max., 30; sternum, 18; vertebra, 16; rib, 12; femur, 11; humerus, 10; pelvis, 9; scapula, 4; zygoma, 1; clavicle, 1; palate, 1.

v. Eiselsberg has called attention to this, that bone metastasis is not prone to generalized dissemination, but is usually quite local.

Teratoma of the Thyroid Gland. Herb[1] reports such a thyroid tumor and states that he has found reference in the literature to seven other cases. The mass extended over the entire left side of the neck. It was apparent at birth. Histologically, nerve tissue predominated. Central nervous tissue, with central channel-like formations, showed. Plexus and epidermal growths like sebaceous cells were noted. Thyroid follicles, mucus producing glands and cavities lined by ciliated epithelium could be recognized. Connective tissue and elastic fibers and blood vessels were demonstrated. The writer refers to the great frequency with which congenital tumors situated near the central nervous system contain nerve elements.

Infection in Tuberculosis. Schroeder and Cotton[2]

(1) American Jour. Med. Sc., June, 1906.
(2) Bureau of Animal Industry, Bulletin No. 86.

throw much light on different phases of the question of tubercular infection, especially through food. They conclude that the gastro-intestinal tract has a good deal of immunity to tuberculosis. Guinea-pigs fed with virulent tubercle bacilli in small numbers for a long time did not become either generally or locally infected. Hogs do not have the same immunity and in consequence of this demonstrated difference between the immunity of different animals conclusions as to man must be held in abeyance. Guinea-pigs injected subcutaneously always become tubercular. The feeding experiments were done with three dilutions, designated A, B and C.

Enough of a virulent culture was suspended in sterile water to make it distinctly cloudy. A loop full of this suspension was transferred to 10 c.c. of milk. This was called A. A loop of the original suspension was transferred to 10 c.c. of water and a loop of this water was transferred to 10 c.c. of milk; this was called B. A transfer of the first suspension to 100 c.c. of water and a loop full of this in 10 c.c. of milk gave C. In neither B nor C would the centrifuge and microscopic examination show the presence of any tubercle bacilli. Of the guinea-pigs fed once with A one-third became tubercular. All those fed for 30 days with A were infected. None of those fed with B and C were infected. Schroeder and Cotton think it probable that B and C contained as many tubercle bacilli as the milk from tubercular cows with sound udders. A study of the location of the lesions in these guinea-pigs convinced the experimentors that the location of the lesions is never an indication of the site of original infection. Woods Hutchinson[1] has made interesting observations on this point. In none of these guinea pigs infected by feeding were there any lesions in the intestines. A series of hogs were inoculated subcutaneously in the abdominal wall near the navel; most of the lesions were found in the lungs; the liver was next in importance. The remaining organs were practically negligible. Schroeder and Cotton think this predilection for the lungs is due to the emptying of the thoracic duct on the portals of the pulmonary circulation and is not held to be selective in any way. They do not discuss the

(1) British Medical Journal, 1899.

question whether or not the lung is an excretory organ for tubercle bacilli. They do not discuss the prominence of liver tuberculosis. As great as is this disproportion they think it even greater in fact. The ordinary infection starts with one or more small foci and the non-infected organs become in some measure immune. Immunity to tuberculosis, both general and local, can be secured by small dosage with mild bacteria. The massive dosage of experimentation does not allow opportunity for the acquisition of immunity.

To demonstrate the filtering power of the lungs they injected two rabbits and a horse with lamp black and recovered the pigment exclusively in the lungs. Even where tubercular lesions were found in the lymph glands no anatomic reason for the selecting of some and the skipping of others could be seen. In fact, location was in no sense a question of anatomy.

Disseminated Tuberculosis in Relation to the Thoracic Duct and Vascular Tubercles. What is the method of infection of the blood stream in miliary tuberculosis? Ribbert[1] thinks that the general infection of the blood stream occurs oftenest through small tubercles in the intima. These are seen best in lungs. The young nodule is frequently primarily located in the media or adventitia and extends to the intima. It may be primarily an abrasion of the intima with a thrombus, in which there is progressive organization and covering with endothelial cells. Such tubercles are prone to shed bacilli into the blood stream. Whipple[2] thinks that this explanation of the very acute forms of miliary tuberculosis is probably correct, but that in the subacute forms, which are more frequent, the infection does not occur through the tubercles. These intimal tubercles are usually covered by endothelium and in addition a thrombus covering forms, so that they are pretty well walled off. The more probable explanation of these is infection through the thoracic duct. During the last year in Johns Hopkins Hospital Whipple has examined smears made from the thoracic duct fluid in all cases of tuberculosis. The method pursued was as follows: A small slit was made

(1) Deutsche med. Woch., 1906, No. 1.
(2) Johns Hopkins Hospital Bulletin, Aug., 1906.

in the upper portion of the duct and a probe was inserted. The fluid was expelled by pressure from the receptaculum up. Thus from 1 to 5 drops was obtained for smears. In two cases of acute miliary tuberculosis, one due to a tuberculous thrombus of the pulmonary vein and one to a caseating aortic tubercle, there were many bacilli in the smears. In 19 cases of subacute tuberculosis, tubercle bacilli were found in the smears in 14. All of the 14 had caseated mesenteries and 11 had tubercular ulcers of the intestines. In six cases of chronic tuberculosis there were no bacilli in the thoracic smears.

Similar views are expressed by Longcope,[1] who observed 30 cases of generalized tuberculosis. In 19 of the cases the type was acute. In 14 of these lesions of the thoracic duct were demonstrable and in one in which there were no lesions of the duct bacilli were found in smears made of the duct fluid. In eight subacute and chronic cases the duct did not show the same preponderance of infection, since lesions thereof were determinable in only two of the cases. In three chronic cases confined to the lungs and peritoneum the duct was found intact. It will be noticed that the relation between duct infections and acute and subacute infections did not coincide in the observations of Longcope and Whipple.

Hematologic Studies in Tuberculosis. Klebs and Klebs[2] quote Kjer Peterson[3] as saying that the normal leucocyte count in men is 4,000 to 5,000 and is relatively uniform. In women it normally ranges from 3,000 to 24,000. They quote Stein and Erbman[4] as follows: (1) Increase of leukocytes in tuberculous individuals, if there is not present a chronic purulent or exudative inflammatory process, speaks for cavity formation in the lung. (2) The beginning of cavity formation in a case can be determined by consecutive counts of the leukocytes and by a sudden increase in their number after a prolonged normal period. (3) Cavity formation can be excluded in most cases if normal numerical conditions are found. The increase of the leucocytes is not due to the tuberculous virus as such, but is a consequence of septicemia caused

(1) Bulletin Ayer Laboratory, June, 1906.
(2) Am. Jour. Med. Sc., Oct., 1906.
(3) Die Leukocytose bei der Lungentuberculose, Würzburg, 1906.
(4) Deutsche med. Woch., Sept. 27, 1906.

by certain highly virulent bacteria, not by what is usually understood by mixed infection, which can not with certainty be excluded in any form of tuberculosis. Arneth has attempted to classify the neutrophilic leucocytes according to the lobulation of the nucleus. The rounded nucleus forms he classifies as I and calls myelocytes. Two-lobed nuclei are II, etc. The claim is made that lobulation of the nucleus is a result of maturity and retrogressive change in the cell. Perhaps something can be gained by classifying polynuclear leucocytes along these lines. Klebs and Klebs think that with increase in the total leucocyte count there is relative increase in the forms with more complicated nuclear arrangement. It is interesting to note that the thirty-two cases of advanced tuberculosis studied by them had an average total leucocyte count of 11,287.

Laffont[1] says that the pulp of organs of tubercular animals heated for some time at a temperature less than 70° C. has curative action in tuberculosis.

Kinghorn and Twichell,[2] continuing the study of agglution after the method of Courmont, conclude that the serum diagnosis of tuberculosis is not a specific sign of the presence of clinical tuberculosis and is therefore of no value. Healthy and tuberculous serums have practically the same agglutinating property.

Hyperplastic Tuberculosis of the Intestines. Nancrede and Butterfield[3] report a case of tuberculosis of the intestines in which there was an enormously productive inflammatory process in the serosa, with some involvement of the other coats as far as the submucosa. There was minimum tendency to necrosis.

Pathologic Calcification. Wells[4] is of the opinion that pathologic and physiologic calcification are quite similar in character. This opinion is not based upon chemical facts, since in the investigations of these he has not succeeded in establishing anything definite. That the calcium is not in combination with fatty acids he is quite certain as the result of many analyses. That there is calcification

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(1) Le Progrés Medicale, March 24, 1906.
(2) Amer. Jour. Med. Sc., Oct., 1906.
(2) Surgery, Gynecology and Obstetrics, Aug., 1906.
(4) Jour. Med. Research., April, 1906.

in necrotic tubercular lesions and none in necrotic syphilitic lesions, and at the same time fatty acids are developing in the former and not in the latter, is suggestive of relationship. It is possible that the calcium soaps are only an early form of combination, which is presently replaced by more stable combinations with phosphates and carbonates. In spite of these superficial arguments he finds so many adverse facts that he concludes that the calcium compounds are not salts of fatty acids. Nor is the salt a compound with phosphoric or carbonic acid. The theory that on the one hand the degenerating nuclei splits off phosphoric acid from its lecithin and that on the other the growing nuclei secrete a loose phosphorus compound is also attractive, but Wells found neither chemical nor other facts to sustain it. For example, calcium was no more readily deposited in tissue rich in nuclei and therefore in lecithin phosphorus than in relatively acellular tissues or in tissues of either type dead.

On the other hand, certain hyaline tissues, such as cartilage, elastic tissue, hyaline infiltrated tissues, seem to attract calcium salts for some unexplained reason. Perhaps the action is simply physical. At any rate, whether the process be the formation of normal bone in normal bone areas, or the formation of metaplastic bone in such osteoporotic processes as osteomalacia or the presence of calcification in necrotic areas the technique is largely the same. Oftentimes it is possible to say definitely this is ossification and that is calcification, yet oftentimes the processes develop together, and as Paschariss ky has shown, areas of pathologic calcification often demonstrate metaplasia into true bone with Haversian canals, lacunae and even marrow.

SPECIAL PATHOLOGY.

BLOOD. ORGANS OF THE THORAX.

Classification of Cells Found in the Blood. G. H. Scott[1] prepared blood films by holding them for 5 seconds in formalin vapor and dropping them while still wet into absolute alcohol. They were then stained with Jenner's

(1) Journal of Path. and Bact., January, 1906.

stain for two minutes, washed in distilled water, rapidly dehydrated in absolute alcohol, cleared in xylol and mounted in xylol balsam, care being taken not to let the film dry at any stage. He arrives at the following conclusions:

1. The classification of the cells of the blood with their source is made complete by the identification of two cells: the basophile cell of marrow, as the source of the basophile leucocyte; and the hyaline cell of marrow, as the immature form of the hyaline leucocyte.

2. The so-called large lymphocyte, which is seen in lymphatic leukemia, especially in some cases, with hyaline leucocytes, is the hyaline myelocyte.

3. Metchnikoff, Kanthack and Hardy and others consider that the lymphocytes are the young forms of hyaline leucocytes.

Ehrlich says they are distinct from each other, and that forms transitional between them are not seen. The writer's observations confirm Ehrlich's view, and he bases his conclusions on the following points of distinction, which appear to be sufficient to enable one to distinguish between the two:

HYALINE LEUCOCYTES.	LYMPHOCYTES.
Size, 10 to 11 μ; also smaller forms, 8 μ. The nucleus with its convexity near one side of the cell measures 7 to 9 μ.	Size, 6 to 8 μ. The nucleus, often in center of cell, measures 5 to 6 μ.
Most often kidney-shaped or with three bulgings, especially in smaller forms. (This would appear round in dry films.) Seldom round.	Usually round, sometimes oval, least commonly notched.
Stains lightly, with indefinite network.	Stains deeply, with marked chromatin network and nuclear membrane.
Protoplasm has opaque appearance of ground glass.	Protoplasm is transparent.

4. The previous classification of the other leucocytes and their source is confirmed.

5. So also are Ehrlich's views as to an embryonic type of blood formation, in which megaloblasts produce megalocytes; and an adult type, in which normoblasts are the source of the normal red blood corpuscles.

6. The blood cells with their source may be stated as:

Leucocytes.

IMMATURE FORMS.	MATURE FORMS.
1. The finely granular eosinophile (neutrophile) myelocyte.	The finely granular eosinophile (neutrophile) leucocyte.
2. The coarsely granular eosinophile (the eosinophile) myelocyte.	The coarsely granular eosinophile (the eosinophile) leucocyte.
3. The basophile myelocyte.	The basophile leucocyte.
4. The hyaline myelocyte.	The hyaline leucocyte.
5. The lymph cell of adenoid tissue.	The lymphocyte.

Erythrocytes.

IMMATURE FORMS.	MATURE FORMS.
In the embryonic type of blood formation:	The megalocytes.
The megaloblasts in the marrow.	The normal red blood corpuscles.
In the adult type of blood formation:	
The normoblasts in the marrow.	

Normally, only the mature forms of leucocytes and red blood corpuscles are seen in the blood, but in certain pathologic conditions any of the immature and the embryonic forms may appear.

7. Each of the varieties of cells described is distinct from its origin onwards. Transitional forms from one type of cell to another are never seen.

8. Lymphocytes are not young forms of other leucocytes; there are immature and mature lymphocytes.

9. Leucocytes do not grow larger as they become mature; they shrink and become diminished in size. The lymphocytes may form an exception to this rule.

10. Neither myelocytes nor nucleated red corpuscles (either megaloblasts or normoblasts) undergo further development into the mature form once they have made their way in the circulating blood. Being foreign elements, they are filtered out by the spleen, and are the cause of the splenic tumor in leukemia, as pointed out by Muir.

11. None of the cells, except the degenerating forms, which appear in the blood in disease are abnormal in character, but only in situation. Even the megaloblasts and megalocytes, which do not normally exist anywhere in the adult body, are always present in early fetal life.

12. Theory.—That the biconcave form of the red blood corpuscles is due to the absorption of the nucleus of the antecedent normoblast.

13. Normoblast nuclei are practically never seen in process of extrusion in wet films, though this appearance is of common occurrence in dry films from the same case; they are, therefore, artificially produced. The free normoblast nuclei are the surviving remnant of degenerated dying normoblasts.

14. The writer has also been able to recognize free megaloblast nuclei, the result of degeneration of the protoplasm of megaloblasts, as well as the more characteristic nucleus of the normoblast.

15. The dots in some red corpuscles, which stain with methylene-blue, are the product of degeneration of the nucleus of normoblasts as well as of megaloblasts.

16. All megaloblasts and normoblasts in the blood undergo degeneration, both nucleus and protoplasm, more or less simultaneously. The megalocytes and normocytes are always produced in the marrow, and not in the blood.

17. Normoblast nuclei are seldom seen in process of degeneration, because they are adult nuclei when the normoblasts enter the blood. The nuclei of megaloblasts, on the contrary, are often seen in this stage, because they are young embryonic delicate nuclei.

18. Polychromatophilia is of two kinds, one signifying that the cell is young and immature; the other that it is

undergoing degeneration. The appearances presented in these two forms are different.

Iodin Staining Granules. Habershon[1] thinks that the iodin granules in certain leucocytes are composed of glycogen, or at least of some carbohydrate body in loose combination with the proteid substance of the leucocyte. They probably originate in the liver and represent the attempt of leucocytes to transport a rather insoluble form of carbohydrate. The granules are rather readily extruded. Habershon suggests some relationship to the eosinophiles. He suggests that the eosin staining granule is the proteid part of the molecule, the carbohydrate part of which stained with iodin.

Hodgkin's Disease and Eosinophilia. Longcope[2] reports a case of eosinophilia and Hodgkins' disease dying from suffocation and coming to autopsy. The number of leucocytes was 13,200, of which 13.2 per cent. were eosinophiles. There were no intestinal parasites. A biologic study of a gland showed a large number of eosinophiles, rather unevenly distributed. He was of the opinion that the eosinophiles were formed in the bone marrow and that the number in the glands was due to accumulation. He saw no evidence that they were being produced there. A count of one thousand marrow cells showed as follows:

	Per cent.
Neutrophilic granular myelocytes	16.9
Transitional neutrophilic granular myelocytes	3.2
Eosinophilic granular myelocytes	12.
Polynuclear neutrophilic leucocytes	37.3
Polynuclear eosinophilic leucocytes	2.4
Small mononuclear lymphocytes	7.8
Large mononuclear lymphocytes	2.
Unidentified	4.4

A differential count of a thousand cells from the bone marrow of a woman dying from an indifferent cause was:

Neutrophilic granular myelocytes	13.9
Eosinophilic granular myelocytes	0.6
Polynuclear neutrophilic leucocytes	50.4
Polynuclear eosinophilic leucocytes	1.2

(1) Journal of Path. and Bact., January, 1906.
(2) New York Med. Journal, May 19, 1906.

It will thus be seen that in this case of Hodgkins there was an increase of eosinophiles in the bone marrow.

Hodgkin's Disease and Lymphosarcoma. Since the enlarged lymph nodes were first studied a great deal of confusion has prevailed concerning the exact relationship between Hodgkin's disease and leukemia, malignant neoplasms, tuberculosis and syphilis. H. W. Gibbons[1] studied nine cases of Hodgkin's disease with the object of determining the relationship of this disease to malignant growths. Three of the writer's cases manifested an undoubted malignant character by affecting not alone lymphoid tissue but infiltrating and destroying adjacent structures. Post-mortem examinations were made in six cases, and the writer had opportunity to study the organs of five. Careful microscopic examinations were made of all growths and the findings of earlier writers confirmed. All five cases showed involvement of lymph-glands all over the body, with metastases in the liver and spleen in four, in the kidney in two, and in the lungs, pericardium, pancreas in one each.

The nature of the disease is uncertain as yet. Some writers consider it a malignant process, but most recent writers believe it to be an infectious process of the character of a granuloma. The points which favor the infectious theory concerning this process may be listed as follows:

1. The clinical picture; the disease may run an acute or a chronic course, accompanied by fever.
2. The frequency with which the disease starts in the cervical glands, suggesting an infection from the throat or skin.
3. The disease may remain quiet, then break out suddenly and cause death.
4. One tissue only, the lymphoid, is affected.
5. The process spreads from a group of affected glands to those nearest it.
6. Final stage of cachexia, diarrhea, hemorrhages, etc.
7. Beneficial effects of arsenic in the treatment.
8. Histologic appearance of the growth resembles that of an infectious process.

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(1) Am. Jour. of Med. Sc., vol. CXXXII, No. 5, Nov., 1906.

9. The lack of infiltration of the capsule and surrounding tissues.

10. Metastases are caused not by cellular transplantation but by proliferation of pre-existing lymphoid tissue apparently anywhere in the body.

Gibbons is led by a careful study of his cases to incline strongly to the malignant theory. He points out that many of the facts listed above belong to malignant tumors as well as to infectious processes. Other facts, such as the beginning of metastases in pre-existing lymphoid tissue in the organs, are not conclusively proven. As to the spread of the process, the writer asserts that not only do the capsules not remain intact in most cases but in many instances an extension beyond the capsule occurs, and in some cases very evident infiltration of adjacent structures. According to Gibbons, Hodgkin's disease should be classified with malignant tumors.

Intraocular Lipemia with Diabetes. Turney and Dudgeon[1] report a case in which the vessels of the fundus seemed to be filled with milk rather than blood. The urine showed a large quantity of sugar. There was no aceto-acetic acid and no acetone, but a few days after dieting was inaugurated these appeared and persisted until the patient died. The fat in the blood was very finely subdivided, probably due to considerations of physics. Staining with Scarlach R. showed fat in all the organs of the body. Osmic acid stained the fat very indifferently, not nearly so satisfactorily as Scarlach. At the autopsy no method revealed any fat in the blood, although it was abundant in that tissue before death. The fat of the body generally was shiny. The pancreas showed a diffuse degeneration. No Langerhans islands could be demonstrated. He quotes Hale White[2] as having seen an exactly similar case.

Latent Pneumococcemia. Wolf[3] shows that pneumococci persist in the blood of pneumonia patients for days after the crisis. The pneumococci recovered from the blood in these conditions are just as virulent as pneumococci from the same blood before the crisis. How long virulent

(1) Journal Path. and Bact., January, 1906.
(2) Lancet, 1903, Vol. 10.
(3) Journal Infect. Dis., May, 1906.

pneumococci can remain in the blood he is not prepared to state. He thinks that crisis is due to something other than disappearance of pneumococci from the blood.

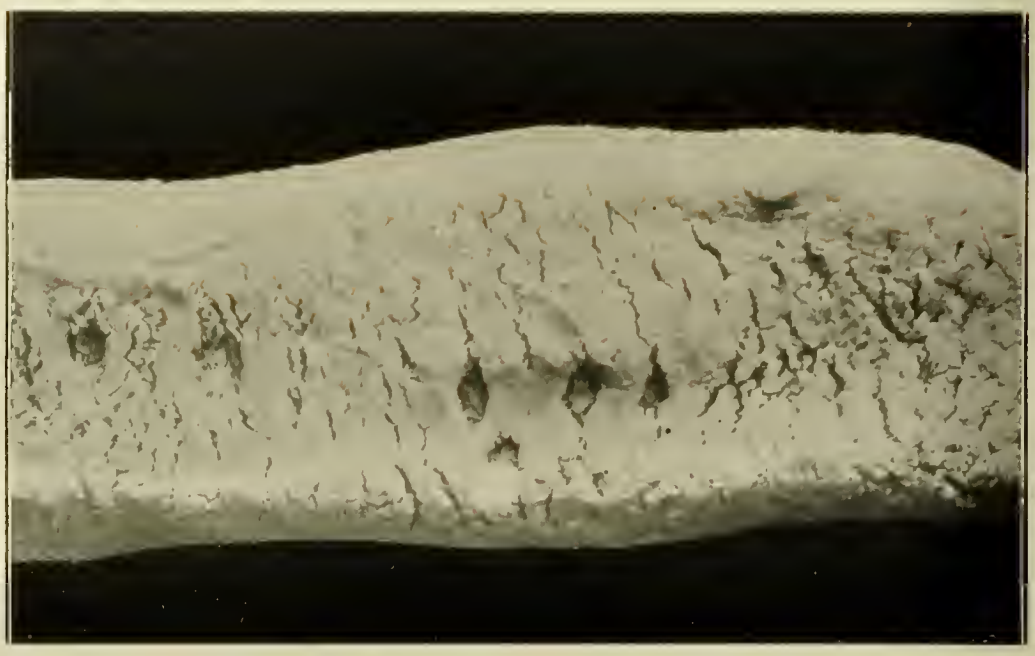
Experimental Arteriosclerosis. Bernhard Fischer[1] experimented with adrenalin and digalin in the production of arteriosclerosis. He found that these agents produced changes in a two-fold way. They poisoned local areas, producing death of some histologic elements and overgrowth of others, and secondly, they operated by increasing blood pressure. The media gave way and a growth of new tissue occurred in the media. It did not invade the intima. The amount of sound tissue outside it determined whether it was to be a yellowish curdy raised placque in the lumen of the vessel or was to originate an aneurysmal area. Fischer did not find that a slowing of the current of blood due to dilation was followed by a thickening of the wall, as Thomas had claimed. Such a growth of fibrous tissue was always inflammatory, never compensatory.

POISONING.

Chronic Acetanilid Poisoning. Herrick and Irons[2] characterize the symptoms of chronic acetanilid poisoning as follows: Cyanosis, that may be extreme; more or less dyspnea and general weakness; dark colored urine that contains paramidophenol and an increased amount of etherial sulphates; anemia of the secondary type, with degenerated and nucleated red blood corpuscles; methemoglobin may be present in the blood and in the urine; dizziness, syncope, tinnitus and palpitation may be marked when the anemia is advanced. The spleen is often enlarged. Anorexia, nausea, vomiting, and diarrhea may occur. Nervousness and restlessness are aggravated when the drug is withdrawn.

Intravenous Injection of Nicotin. Adler and Hensel[3] injected rabbits intravenously with a solution of 1½ milligrams of pure nicotin in water daily for one to two months. They got atheroma lesions in the aorta. The lesions begin as a degeneration of the muscle fibers next

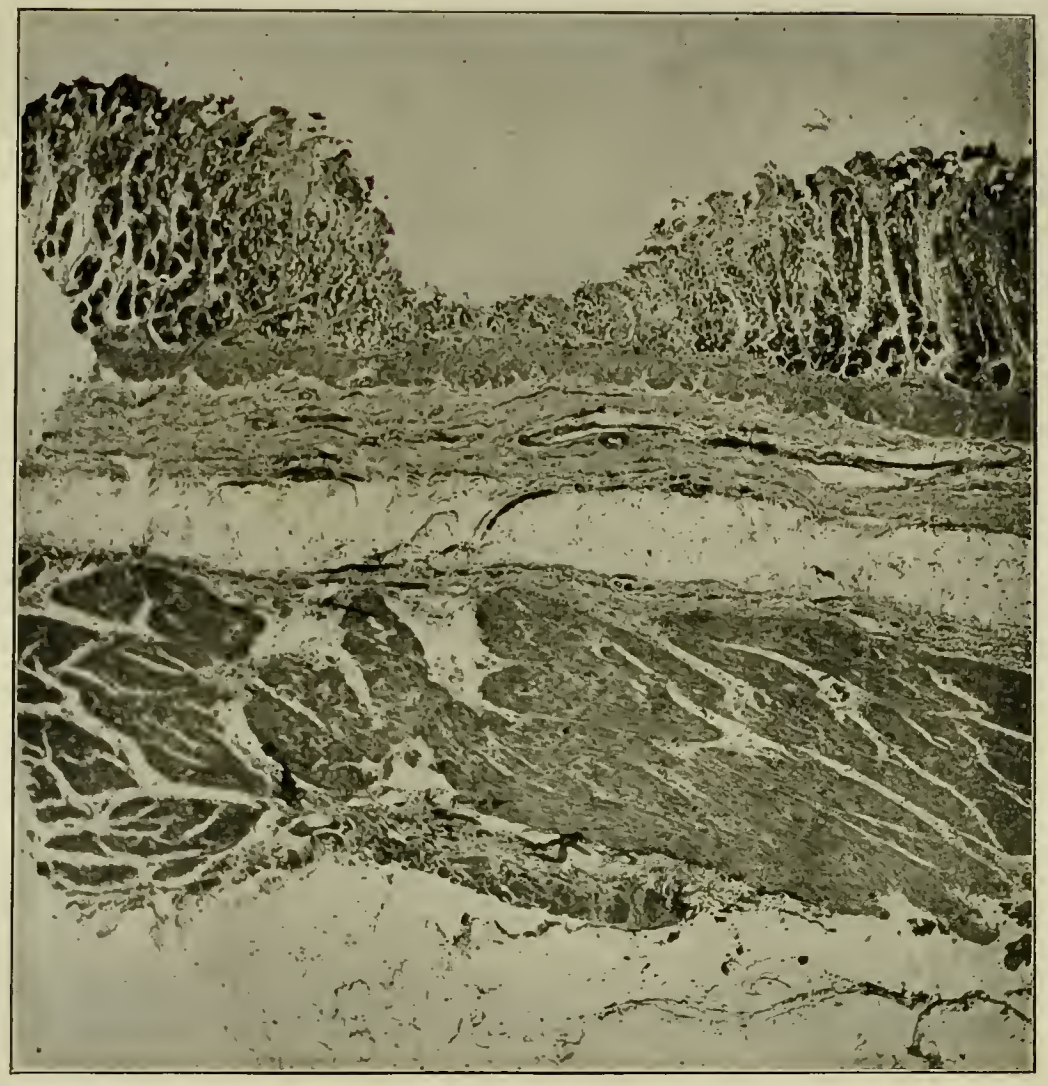
(1) Deutsche med, Wochenschr., vol. XXXI, 1905.
(2) Jour. Am. Med. Assoc., Feb. 3, 1906.
(3) Jour. Med. Research, September, 1906.



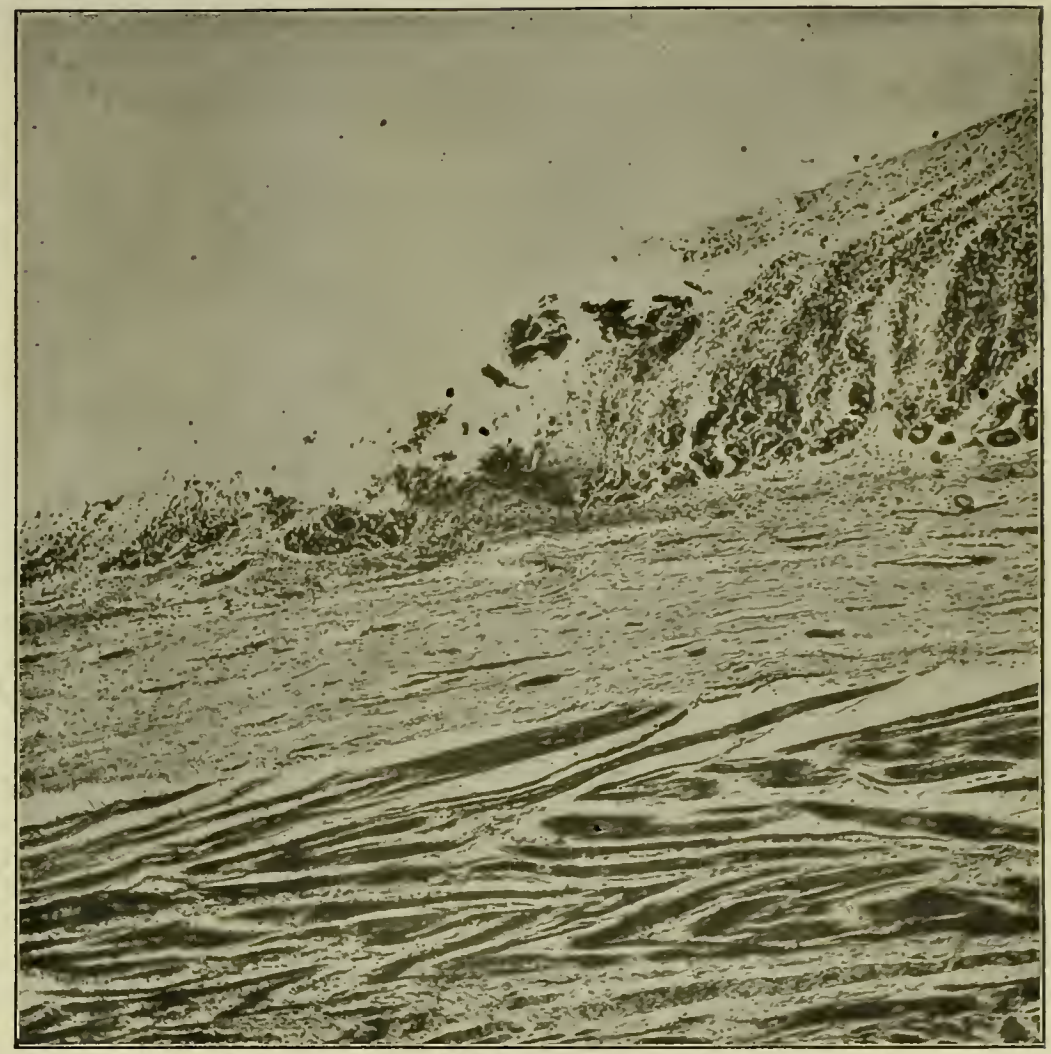
Deep peptic ulcer of duodenum. (First portion.)

Deep ulcer in which perforation occurred, resulting in general peritonitis and death.

PLATE II.



Stomach of dog. Moderately advanced stage, with necrosis reaching almost to the muscularis, exposing a small blood vessel (low power).



Stomach of dog. Edge of ulcer reaching to the muscularis, showing marked degeneration changes with breaking down of the entire glandular structure (low power).

PLATE III.

the intima. These fibers speedily went to pieces and were the site of calcareous deposit. The changes in the elastic fibers were mechanical and due to the weakening of the muscle and the presence of the lime masses. The changes in the adventitia and in the connective tissue of the media were wholly secondary. Some of the areas of necrosis and calcification formed aneurismal pouches and some formed white patches which projected into the lumen. It will be noted that exactly similar lesions were produced by injecting digalin and adrenalin. Adler and Hensel think that these experiments explain the origin of atheroma, aneurism and perhaps also of arteriosclerosis in the human subject. The variations in appearance are due to intercurrent factors.

Influence of Tension on the Degeneration of Elastic Fibers. Harvey[1] experimented in order to determine the resistance to degeneration of elastic fibers and the relation of tension thereto. The question is interesting by reason of the conflicting observations of those studying the histology of tumors and such granulation tissues as those of tuberculosis and syphilis. He concludes that elastic tissue is relatively very resistant to degeneration. This power of resistance is lowered when the tissue is placed under tension. When not under tension the fibers degenerate after the following order: 1. Fibrillation. 2. Loss of staining power. 3. Fragmentation and granulation. 4. Diffuse staining. 5. Calcification. Under tension they degenerate by thinning and then by absorption. They never calcify.

Histologic Changes in the Myocardium After Injections of Adrenalin. Pearce[2] injected adrenalin intravenously and examined the hearts closely for finer changes. Some of the animals died after one injection. These showed wide dilatation of the ventricles and marked edema of the myocardium. The edema served to make manifest the branching of the heart muscle fibers. In those animals which survived until a fourth or fifth injection, the muscle fibers were edematous and showed hyaline and granular degeneration, but no fatty changes. The dilatation of the cavities was marked. Those standing more than fifteen

(1) Jour. Exp. Med., May, 1906.
(2) Jour. Exp. Med., May, 1906.

injections showed patchy proliferation of connective tissue. This was usually perivascular. It was often found in the papillary muscles.

Pearce thinks the changes due to ischemia from contraction of the arterioles. He noted, as has Zeigler, that the changes are most pronounced just at areas of the frailest blood supplies, areas of relative physiologic ischemia. He thinks these lesions are akin to those in man in those cases of sudden death associated with acute dilatation of the heart. He thinks there is no relationship to the commoner chronic forms of myocarditis.

Pearce and Baldauf[1] produced lesions in the aorta of rabbits by injecting a single large dose of adrenalin. The animals were injected with ½ to 1½ minims of the drug. After the lapse of about two months they were killed and calcareous patches were found in the aorta. Histologic examination showed an extensive and diffuse degeneration of the media, with more or less complete necrosis of the muscle cells and a straightening and fusion of the elastic fibers, with a few angular bends. About two-thirds of the circumference of the vessels was involved, and transversely the middle third of the media. In the heart muscle were focal areas of degeneration, with slight increase of connective tissue and accumulation of lymphoid cells. They quote Loeb and Githens[2] as holding that time was more of a requisite than multiplicity of doses, yet they are the first to produce such lesions with a single dose.

Calcification of the Media in Arteries. This condition has been found by Moenkeberg[3] in the vessels of the extremities in old people. Frequently the process of calcification involves these vessels alone, on which clinicians base the diagnosis of arteriosclerosis, while the aorta and its main branches remain unaffected. Klotz[4] detected primary calcification of the media in arteries of the elastic tissue type in several old people. He has seen the condition in three cases under 45, namely, 39, 41 and 43 years of age respectively. In old people such deposits of calcium

(1) Am. Jour. Med. Sc., Nov., 1906.
(2) Am. Jour. Med. Sc., Nov., 1906.
(3) Virchow's Arch., 1903, vol. CLXXI, p. 141.
(4) Jour. Exp. Med., vol. VIII, No. 2, March 26, 1906.

salts in the media of vessels of elastic tissue type may be said to be the rule. The condition is present in fully one-third of those over 50 years of age.

The writer was led to the discovery of these facts by considering the detection of pathologic quantities of calcium by the naked eye as unreliable. He had seen often that microscopic calcium deposits were found where macroscopic examination gave entirely negative results and resolved to use the latest methods at our command for the detection of calcification. The results were that specimens of aorta which were pliable and elastic and apparently normal to the naked eye, when examined in microscopic sections, showed the media to be loaded with calcium salts.

A description of the calcium deposits in the intima, as observed by the writer, shows that the process is similar to that previously reported as occurring in the arteries of the extremities, which are vessels of muscular type with the difference that in the writer's cases the process was observed in the media of vessels of the elastic tissue type, the vessels chiefly involved being the aorta and the carotids, innominate, and subclavian arteries. It also differs from the process observed in the media of vessels of muscular type, in that it is limited to the granular stage of degeneration and involves only the muscle fibers, leaving the elastic fibers unaffected.

Growth of Lymphatics in Granulation Tissue. Coffin,[1] making use of the ease with which lymphatics in the intestinal wall can be injected, has studied the growth of lymphatics in granulation tissue. A loop of intestine was sewed into a skin wound and left until it was covered with granulation tissue. The animal was killed, his blood vessels injected with material of one color and the lymph channels with material of another. Lymph capillary loops were found growing into granulation tissue just as blood capillary loops do. These loops sprung by endothelial budding from preëxisting lymph channels. The new channeled areas were continued by double walled unchanneled areas and then a single layer of endothelial cells and a prolongation of endothelial protoplasm in the order named, proceeding outward from the preëxisting vessel.

(1) Johns Hopkins Hosp. Bulletin, August, 1906.

ABDOMEN AND PELVIS.

Ulcers of the Stomach, Pathogenesis and Pathology. Fenton B. Turck[1] has succeeded in producing ulcer of the stomach in dogs fed with *B. coli communis* for a variable length of time. Ulcers produced by some form of mechanical injury to the stomach wall heal more readily than in other parts of the body, and attempts to produce ulcer by chemical injury either fail to produce the lesion or the lesion heals more or less promptly.

An anemia is frequently associated with ulcer. Various attempts have been made to produce ulcer by combining anemia and some mechanical injury such as resection of the mucosa with bleeding. If the anemia was sufficiently profound and the injury well marked, ulcers were produced in the stomach. The production of ulcer of the stomach by destroying areas in the brain, or section of the cord or vagi, cannot be satisfactorily explained.

When dogs were fed oil of mustard for 14 months and the stomachs examined, gross and microscopic, showed no ulcers, it was proven that simple irritation unassociated with other etiologic factors would not produce peptic ulcers of the stomach or intestines.

From the feces of clinically diagnosed cases of ulcer of the stomach cultures of bacillus coli were made. These cultures were fed to dogs for periods of time varying from 81 to 102 days. Examination, post-mortem, of the stomachs of these dogs showed peptic ulcers in all cases. The ulcers were multiple. The ulcers had the gross and microscopic appearance of peptic ulcers. (See Plates II and III.)

The bacteria fed were identical morphologically and culturally with strains of coli isolated from the stools of normal individuals. The possibility that there might be pathogenic or other biologic differences not determinable by any ordinary means led Turck to make use of cultures from cases of stomach ulcer. Since the toxin of bacillus coli is intracellular and fixed quite firmly, it is suggested that possibly the same effect could be produced with dead colon bacilli. The number and extent of the ulcers found

(1) Jour. Am. Med. Assoc., June 9, 1906.

in the dogs varied from a few ulcers of the duodenum to numerous typical ulcers in the stomach. One dog died from a hemorrhage due to a large ulcer situated near the pylorus.

Gastric Ulcers in Rabbits. Following the experimental work of others, W. Ophüls[1] produced gastric ulcers in rabbits by resecting both vagi below the diaphragm. Thirty rabbits were operated upon and the results were positive in six. The first ulcer was found on the twenty-fourth day following the operation, and if the animals examined before that day are excluded from the count the results are six positive and twelve negative cases.

All ulcers were single. Van Yzeren,[2] who made similar experiments, reported several instances in which they were multiple. The marked induration at the base of the ulcers showed that they were chronic. They were of round or oval form, with sharp edges and smooth bottom. In one case ulceration extended into the muscle, while in another it reached the subperitoneal tissue. The base of these two ulcers showed a considerable amount of cicatricial tissue covered with a thin layer of necrotic material, including fibrin, blood, remnants of food, etc. Some ulcers showed extensive hypertrophy of the mucous membrane at the edge, and in such instances the mucous membrane projected over the ulcer. All larger arteries and veins in the neighborhood of the ulcer were entirely normal.

It may be seen from these facts that resections of both vagi below the diaphragm in rabbits is followed by peculiar chronic ulcers beginning in the mucous membrane of the stomach, but that this result is neither constant nor remarkably frequent.

The writer discusses the relation between the resection of the vagi and the production of ulcers. Van Yzeren, claiming to have observed the occurrence of cramps in the stomach muscle after resection of the nerves, ascribes to this fact the origin of the ulcers. Ophüls maintains, however, that no such cramps occur; he only found a temporary dilatation of the stomach in the operated animals so that it could be easily palpated through the abdominal wall, the dilated and overfilled organ being felt as a very hard mass.

(1) Jour. of Exp. Med., vol. VIII, No. 1, Jan. 25, 1906.
(2) Zeitschrift f. klin. Med., 1901, vol. XLIV, p. 181.

The stomach gradually regains its normal tone and it is this temporary condition which, the writer believes, may have misled Van Yzeren and induced him to presume that tonic cramps of the muscles occur after resection.

Ophüls inclines to believe that the ulcers are traumatic in origin and are due to the mechanical injury caused by hard, more or less pointed substances in the food. The occurrence of the ulcers upon the highest point of a projecting fold of the mucous membrane favors this view. Hemorrhages and erosions were occasionally found by the writer in the stomach of control animals; it appears that section of the vagi below the diaphragm simply favors the development of chronic ulcers, while the ordinary, mechanical injuries to the stomach wall have a tendency to heal rapidly.

The Vermiform Appendix of Man. R. J. A. Berry[1] has shown that the vermiform appendix of man is represented in the vertebrate kingdom by a mass of lymphoid tissue and that the latter is the characteristic feature of the cecal apex. The lymphoid tissue at the cecal apex tends to be collected together into a specially differentiated portion of the intestinal canal as the vertebrate scale is ascended until the vermiform appendix is formed in the higher species. It must be concluded, therefore, that the vermiform appendix is not a vestigial structure but, on the contrary, a specialized part of the alimentary tract, characterized by its lymphoid tissue.

R. J. A. Berry and L. A. H. Lack[2] have made extensive researches to determine at what age lymphoid tissue first appears in the human appendix and at what age, if at any, does the lymphoid tissue tend to disappear. These points, if settled, would settle the question whether obliteration of the human appendix is a physiologic process, as affirmed by Ribbert, or a pathologic condition as affirmed by others.

Numerous sections have been made of 103 human appendices of both sexes and all ages, ranging from the full-term fetus up to eighty years; they were stained chiefly with hemotoxylin and eosin.

In his first paper, Berry had shown that although the

(1) Jour. of Anat. and Physiol., n. s., Vol. XV, p. 83.
(2) Jour. of Anat. and Physiol., Vol. XL, part III, 1906.

rabbit's appendix contains very little lymphoid tissue at birth, the latter is increased so rapidly that the appendix is converted practically into a lymph-gland within one week. The same holds true of the cat and pigeon, and in the present series of investigations the writers observed that it is true also of man, with the difference that the time required for the evolution of lymphoid tissue in the appendix of man is somewhat longer, namely, a month to six weeks.

There is a great deal of similarity, therefore, in the appendix of man and the cecal apex of lower animals; both are comparatively free of lymphoid tissue at birth and in from one to six weeks become converted into an actively functional lymph-gland.

In order to determine whether the lymphoid tissue tends to disappear from the human appendix, the writers have divided all the normal appendices examined into decades and have counted the number of follicles in each section. The average number of lymphoid follicles present in a single transverse section through the center of the human appendix was found to be as follows:

Below one year	5
Between the ages of 1 year and 10 years	6
Between the ages of 10 and 20 years	7
Between the ages of 20 and 30 years	6
Between the ages of 30 and 40 years	3
Between the ages of 40 and 50 years	3
Between the ages of 50 and 60 years	2
Between the ages of 60 and 70 years	Traces only
Between the ages of 70 and 80 years	Practically none

It will be seen from this table that lymphoid tissue diminishes towards middle life and from that time onwards shows a progressive tendency to disappearance, although it never disappears altogether. A comparison of an appendix from the first decade of life with one from the last decade of an aged person is even more conclusive. For example, the lymphoid follicles in an appendix of a person 19 years of age are more numerous and larger than those of an appendix obtained from a person 80 years of age.

These observations lead the writers to conclude that lymphoid tissue is a tissue of the growing animal. They point out that the amount of lymphoid tissue present at the cecal apex varies, most probably though not certainly, in accordance with the varying diet of the animal.

Obliteration of the Vermiform Appendix. This question is of considerable practical importance. Berry and Lack in the paper referred to above mention that they have found undoubted cases of complete obliteration of the vermiform appendix seven times out of 103 cases. This is contrasted with the statement made by Ribbert, who claims to have met with partial or complete obliteration of the vermiform appendix in something like 25 per cent. of his cases, but never saw a case of complete obliteration below the age of 30 years. Ribbert regarded obliteration as a normal process of involution in an organ undergoing retrogressive changes. Berry and Lack differ with him; of their seven cases, three were in patients below the age of 22. With regard to sex, three occurred in males and four in females. The cause of death was cardiac disease in four cases, Bright's disease, malignant stricture of the esophagus, and phthisis in one case each. All seven cases were submitted for examination to an expert pathologist, who found that in every instance the occlusion was a pathologic process—"an interstitial fibrosis, the result of vascular obstruction, and possibly part of a general arteriosclerotic condition." The writers conclude from these facts that obliteration of an appendix free from appendicitis is not a physiologic process of natural involution as maintained by Ribbert, but is a purely pathologic process, and give their reasons as follows:

1. Obliteration is not confined to the latter half of life, but occurs at all periods.

2. A progressive examination of appendices from birth up to the most advanced periods of life does not reveal any very great increase in the tendency to obliteration.

3. The cause of death in six out of seven cases involved vascular changes with concomitant backward pressure.

4. The opinions of pathologists support the view that all cases of obliteration are undoubtedly pathologic in character.

Pathogenesis, Etiology and Pathology of Peritonitis. Evans[1] says that in the last 1,000 autopsies at Cook County Hospital there were 33 cases of miliary tuberculosis, of which 16 showed intestinal ulcers. Cummings found peritoneal tuberculosis 92 times in 3,405 autopsies at the University of Pennsylvania, and Borshke in 226 of 4,250 autopsies.

Of all cases of peritonitis 70 per cent. are suppurative in character; 25 per cent. are due to tubercle bacillus. The remaining 5 per cent. are about equally divided between capsular peritonitis due to colon bacillus leakage, causing subinfection and a loose group composed of miscellaneous factors of the pus infections. Much the largest number occur through the female genital route. Of the tubercular peritoneal infections 70 to 80 per cent. are in males. Full consideration of this fact would indicate that infection of the peritoneum with tubercle bacilli traveling through the female genital organs is not of much consequence.

In the series of 1,000 autopsies there were 104 cases of tubercular ulcers in the intestines. Twelve of these were in cases recorded as healed pulmonary tuberculosis; 16 were associated with tubercular peritonitis. The other 76 cases were cases of common chronic phthisis without peritoneal involvement demonstrable to the naked eye on routine examination, but without intestinal ulcers. These figures would indicate that the peritoneum is quite tolerant of or well protected against tubercle bacilli.

The subinfections or leakages of mild bacteria such as colon bacilli are responsible for chronic hyperplastic forms of peritonitis, usually quite well localized. In localities where the intestine does not move longitudinally, adhesions are prone to occur. These hyperplasias are best seen on the surface of organs such as the liver and spleen, in and around the flexures of the colon, the head of the cecum and appendix, and the sigmoid. The presence of such adhesions around the appendix do not mean antecedent attacks of appendicitis. They result from bacterial leakage. However, such adhesions may interfere

(1) Illinois Med. Jour., October, 1906.

with the drainage of a narrow tube such as the appendix, and thus result in appendicitis.

Pathogenesis of Ascites. Tieken[1] says that in about 3,000 autopsies at Cook County Hospital ascites was present in 362, or 8.3 per cent., eliminating duplicates. In 49 per cent. of the 362 the ascites was a part of a general dropsy. Cirrhosis of the liver was present alone in 16 cases and associated with heart and kidney disease in 61 cases. It was associated with disease of the heart alone in 27 cases; of the kidney alone in 14; heart and liver, 21; heart and kidney, 70; kidney and liver, 33; heart, kidney and liver, 38; carcinoma within the peritoneum, 49; sarcoma, 8; syphilis of the liver, 18; aneurism, abdominal aorta, 2; tuberculosis of the peritoneum, 25; chronic pericarditis, 4; capsular cirrhosis, 8; endothelioma of the peritoneum, 1. The author says that ascites does not argue for any particular underlying pathology.

Fibroma of the Gastro-hepatic Omentum. Murphy[2] reports a fibroma of the gastro-hepatic omentum situated in the lesser peritoneal cavity posterior to the stomach and springing apparently from the region of the posterior surface of the lesser curvature. He terms it a fibro-myxomyoma telangiectaticum. The blood vessels apparently were acquired from the neighboring structures. The literature shows only tumors primary in the omentum. These were reported by Jackson and Gould.[3]

Vitelline Duct Malformations. Richter[4] found that deviations from the normal in the evolution of the vitelline duct result in malformations that may be grouped in two quite different types of congenital malformation. 1. Congenital diverticula and their remains, congenital bands, etc. 2. Congenital hernia into the cord.

Meckel taught that the true diverticulum was a remnant of the vitelline duct which had not undergone the normal retrogressive changes to complete disappearance. The wall of the duct became the wall of the diverticulum, and the degree of deviation from the normal in the evolu-

(1) Illinois Med. Jour., October, 1906.
(2) Surgery, Gyn. and Obst., October, 1905.
(3) Medico-Chirurgical Transactions, 1900, p. 257.
(4) Surg., Gyn. and Obst., June, 1906.

tion of the duct determined the form taken by the diverticulum.

The communication with the intestine may be closed, the diverticulum forming a cyst usually attached to the free border of the bowel.

A preternatural anus at the umbilicus is associated with the more perfect diverticula whose attachment at the umbilicus has not been closed.

Fistulæ at the umbilicus are not necessarily fecal. They may arise from vitelline remains left in the abdominal wall at or near the umbilicus without any intestinal or intra-abdominal remains persisting. Such a series would have an epithelial lining. The most common source of pathologic disturbance associated with a Meckel's diverticulum is intestinal obstruction.

Hernias into the cord are generally attributed to an abnormally thick or resistant vitelline duct, which, by requiring more time for its disappearance, prevents the normal recession of the gut into the abdominal cavity. The size of the hernia would be influenced by the degree of resistance of the duct. The hernia may include all of the abdominal viscera, and as a result of the absence of its normal contents the abdomen remains undeveloped.

Tropical Splenomegaly. Musgrave, Wherry and Woolley[2] report seven cases of this disease. It is probably the same disease as Quisig, Cayana, Kala Azar and Dum Dum fever. There is a splenomegaly with a profound anemia and some tendency to leucopenia. Differential leucocyte counts showed nothing definite or uniform. Nothing could be found in the way of an animal or vegetal parasite by direct examination or various culture and biologic methods. In one autopsy no well defined lesions could be made out. Sections of the very large spleen showed a chronic hyperplasia, with congestion. Guinea-pigs injected with an emulsion made from some of the spleen died in about four months without special lesions.

Acute Hemorrhagic Pancreatitis Following Obstruction of the Bile Papilla. Bunting[2] reports a case of fat necrosis without much hemorrhage. In addition there was a

(1) Johns Hopkins Hosp. Bulletin, January, 1906.
(2) Johns Hopkins Hosp. Bulletin, August, 1906.

chronic interstitial pancreatitis and an abundance of gallstones. The anatomic conditions fulfilled Opie's laws, namely, Wirsung's duct joined the common duct high enough up so that the ampulla was longer than its diameter at the mouth. In consequence, a stone lodging at the mouth would cause the bile to flow up the pancreatic duct into the pancreatic substance. Santorini's duct was obliterated.

[It seems to the Editor that if the accessory duct were patulous, regurgitation into the pancreatic duct would be helped rather than hindered. Opie was able to produce fat necrosis by sending bile into the pancreatic duct, and Flexner[1] has shown that it is the salts, and especially sodium cacodilate, which is responsible.]

Further Study of Experimental Production of Liver Necrosis by the Injection of hemagglutinative Sera. Reference to Practical Medicine Series for 1905, volume IX, will show the position of Pearce[2] on this question. He thinks, now as then, that various liver necroses and secondary cirrhoses are due to starvation from agglutination of red corpuscles within the capillaries associated with the pressure of perivascular edema. The agglutination is due to agglutinins. Hemolysins and specific cell toxins have no capacity, or but limited capacity, for producing these lesions. As Opie has shown, the peripheral vessels and the vessels around the portal spaces have intravascular pressure enough to prevent plugging by these soft clots. It is in the vessels of the middle and inner third of the lobule that the congestions occur.

Necrosis of Epithelium of the Kidney in Infections and Intoxications. In addition to the acute nephritis in which there is some evidence of reparative reaction, there are cases in which the breaking down of highly specialized cells is so fulminant as to be attended by no effort at repair. Such lesions have been noted especially in the liver. In addition to the more definite acute yellow atrophies Bevan and others have written of degenerations of the liver substance subsequent to chloroform. That similar lesions occur in the kidney is the opinion of Hewlett,[3]

(1) Journal Experimental Medicine, 1906, p. 167.
(2) Jour. Med. Research, April, 1906.
(3) Johns Hopkins Hosp. Bulletin, August, 1906.

who has found 10 cases in 2,500 autopsy records. Of these ten cases, five were associated with rather a typical acute yellow atrophy of the liver, and in one there was a recent pregnancy. There was a blood infection with colon in five cases, streptococcus in seven, aureus in three. Hewlett ascribes the necrosis of the tubule epithelium to severe bacterial action. In the cases of Griffeth and Herringham[1] no bacteriologic examinations were made, and the question of etiology is begged. However, the case occurred in a woman who had just been delivered of a dead fetus, and the interior of the uterus showed a grayish membrane or slough. The presence of thrombi in the cortical veins and branches offers some confirmation of the bacteriologic origin. In this case there was almost complete suppression of the urine for days, without many of the symptoms of uremia. The epithelial degeneration involved the nuclei as well as the protoplasm, neither the nucleus nor the protoplasm taking any stain. In this case there was a good deal of reparative production of new cells by the connective tissues of the affected zone. In the case of Bradford and Lawrence[2] the result was ascribed to an arteritis obliterans. This does not seem probable in the light of more recent observations. Hewlett noted calcareous deposit in the areas of injured tissue. He thinks calcareous infiltration occurs more readily in injured than in dead tissue.

Congenital Cystic Kidney and Liver. Although the subject of congenital cystic kidney has received a great deal of attention, C. H. Bunting[3] reports two recent cases which he had opportunity to study because the lesion was so early that they may throw some light on the pathogenesis of the condition which is quite obscure at present.

Both cases were new-born infants, the first and second children of an apparently healthy negro woman, 16 years of age at the time of the delivery of her first child. The first was a male child and died suddenly on the eleventh day. The second child, a girl, was born eleven and a half months after the birth of the first child and lived 19 days; both were born prematurely, but the labor was normal.

Most cases of congenital cystic kidney reported in litera-

(1) Journal of Path. and Bact., March, 1906.
(2) Jour. of Path. and Bact., 1898, p. 197.
(3) Jour. of Exp. Med., vol. VIII, No. 2, March 26, 1906.

ture showed other lesions in the nature of congenital malformation, such as hydrocephalus, polydactylism, hairlip, hypospadias, atresia of the vagina, vesico-rectal fistula, and some malformations of the internal genitalia. These two cases showed no such malformation, and their organs were apparently normal. Microscopic examination, however, revealed that the liver was in an early stage of cystic degeneration, and in one case the pancreas was equally involved. The association of cystic kidney with similar degeneration of the liver is a common occurrence and is considered by Bunting an important fact to be considered in the question of the pathogenesis of this disease. Luzzatto[1] found the two conditions associated in 43 cases, or 19.11 per cent. of a large series of cases collected from the literature.

Concerning the pathogenesis of congenital cystic kidney, the view that the cysts are formed in the interstitial tissue has been abandoned entirely. The tubules and the glomeruli are variously given as the starting points for the cystic degeneration, and the explanations given for its occurrence may be grouped as follows:

1. That the cysts are the results of obstruction and of retention of secretion. 2. That they are of the nature of a neoplasm. 3. That they are the result of malformation; and, 4. That the condition lies between the last two, partaking somewhat of the nature of each.

The writer points out the difficulty of properly classifying this condition. It differs from the condition usually included under neoplasm, and the term adenocystoma is clearly inappropriate; it cannot be considered a malformation either, except in the sense that, primarily, one finds an active proliferation of the epithelium of the collecting ducts of the medulla and of the junctional tubules in the inner part of the cortex of the kidney.

So-Called "Necrobiosis" of a Fibromyoma of Uterus. F. G. Bushnell[2] reports a case of so-called "red" degeneration of a fibromyoma of uterus and claims that it is due to a subacute form of necrosis. About 5 to 7 per cent. of fibromyomata removed are said to have undergone this degeneration change. The "soft fibroid" of the textbook is an

(1) La Degenerazione cistica dei Reni, Venice, 1900.
(2) Brit. Med. Jour., Oct. 28, 1906.

ordinary fibroid which has undergone this fatty, edematous, cystic, or myxomatous degeneration. Adenomyomata are, however, not included in this clinical class, which has no pathologic basis truly. In appearance they are red or fleshy—softer, looser, more like muscle. On section the color may be pink, light red, purple red, or livid, and diffused throughout the growth, as in the specimen shown. Bland-Sutton says a fibromyoma undergoing necrosis is usually dirty yellow, but it may become deeper, and even dark mahogany, in pregnancy, and in streaks, or evenly distributed. The change usually affects single or interstitial tumors, but W. W. H. Tate has recorded nine multiple ones. The necrotic change usually begins in the middle as a red area, which loses its fibrous appearance, and is softer and more diffluent. There is a sharp distinction between the blood-stained growth and the white capsule of the uterine muscle. The smell is sometimes stale, fishlike. This may be due to the presence of amines, a product of destructive distillation of proteid. There is no excess of fluid or blood found present. Gebhard considers the condition one of necrobiosis or maceration, and as the nutrition runs centripetally, the first change takes place in the central portion. Tissues are softer and the color is due to the breaking up of red cells and diffusion of pigment. In later stages may be brown or greenish. The tumor cells lose their capacity for taking up nuclear stains. The differentiation from tissues around may not be clear. In cases with a pedicle, there is no twisting and there is no external change in growth. No bacteria have been isolated up to the present.

Pregnancy *per se* appears to have an influence on the change, but the ultimate cause is unknown. It is not associated with extreme age. Vautrin suggests that it is an ischemia produced by uterine contractions and by the development of an inextensible fibrous capsule. The condition gives rise to definite clinical signs, such as severe pain, rapid pulse, etc. Microscopically the changes are those of necrosis. There is an absence or deficiency of nuclear staining, leaving bundles of fibers which have taken up the diffuse stain. Sometimes the muscle bundles have a granular or hyaline appearance, and nuclei may lie in clear spaces and be faintly stained.

Multiple Non-Inflammatory Necrosis of the Liver with Jaundice. H. Oertel[1] has described under this title the anatomic and pathologic findings of a peculiar affection of the liver. The process consists of a multiple, irregular, circumscribed solution of liver cells without parenchymatous degeneration or coagulation necrosis and is associated with a corresponding lobular blood and bile stasis in the affected areas. It appears that the protoplasm and later the nucleus of the cells simply waste and dissolve, leaving a more or less well-preserved reticulum with stagnant bile and blood. While undergoing this change the cells show fatty degeneration and finer or coarser bile pigment within their bodies, sometimes reaching a considerable degree. The impression one gains from the appearance of sections is that the process is one of solution or cytolysis of the parenchyma. The central portions of the lobules are the regions most involved. The process appears to originate around the central vein, but is by no means confined to that point, as it occurs also in streaks running from one into neighboring lobules, and is gradually lost in well-preserved liver tissue. One characteristic feature of this process is the absence of any inflammatory reaction anywhere in the liver tissue proper, the portal spaces alone showing sclerosis of a more or less recent date. The sclerotic change is particularly well marked and most mature around the portal vein itself. A moderate peripheral fatty infiltration is discernible. Macroscopically the liver shows no marked decrease in size but appears tough, leathery, pale yellow, bile stained and without its markings. Irregular vascular injection or darker, larger, deep red spots are plainly visible corresponding to the irregular stasis.

Oertel adds three more cases to the one upon which the description of this condition has been based, giving all histo-pathologic findings in detail. From the description of these four cases it appears that they differ essentially from all other process where destruction of parenchymatous cells form the essential feature. Here the protoplasm undergoes no definite process of coagulation or granular disintegration leading to the death of the cell as is seen

(1) Jour. of Exp. Med., vol. VIII, No. 1, Jan. 25, 1906.

Cystic Aplasia.

PLATE IV.

in the case of parenchymatous degeneration or necrosis in Virchow's or Weigert's sense; it only undergoes a fatty change frequently associated with loss of substance, the cell contents manifesting a uniform fading. The cellular outline is lost early in the well-known processes, but here it is well preserved, as is also the ability to secrete bile, which is continued to a late stage. The writer maintains that the proper term for this process is cytolysis, and he looks upon the lesion as positively due to a solution of cells.

The fact that in a little over a year four cases were observed by the writer justifies a suspicion that some cases now classified as irregular stasis or parenchymatous degeneration may belong to this category of lesions.

Experimental Cirrhosis of the Liver. It has been known for a long time that the intravenous injection of hemolitic immune sera caused more or less extensive necrosis of the liver cells, the size and position of the necrotic areas depending upon the amount of serum administered and bearing a direct and very definite relation to thrombi composed of fused red blood corpuscles. The repair process following in animals surviving the acute toxic effects of the serum has been studied by R. M. Pierce[1] in the hope that as the extent of injury where large doses are given is such as to preclude complete repair without formation of connective tissue, the process may shed some light upon cirrhosis of liver in man, which it resembles closely except for a difference in the distribution of the new tissue. He found that the histogenesis of cirrhosis may be studied step by step, and incidentally various repair processes in the liver, but this form of experimental cirrhosis does not elucidate the etiology of cirrhosis in man, nor does it explain the peculiar arrangement of the new connective tissue in any form of human cirrhosis except possibly that associated with chronic passive congestion.

The writer looks upon the reparative process which follows the widespread necrosis of the dog's liver caused by the injection of hemagglutinative serum as a more definite cirrhosis than any other experimental lesion hitherto described. His experiments show that cirrhosis may follow extensive primary destructive lesions, a view not yet fully

(1) Jour. of Exp. Med., vol. VIII, No. 1, Jan. 25, 1906.

accepted, and seem to support the contention of Kretz that cirrhosis is essentially a reparative process.

Toxemic Vomiting of Pregnancy. Whitbridge Williams[1] is of the opinions that to group eclampsia and the liver necrosis of pregnancy together will be a distinct backward step. Besides these there are several other toxemic phenomena, such as the few days of mild coma subsequent to parturition, which demand still other groups. In eclampsia there is thrombosis originating in the portal veins; in liver necrosis there is necrosis of cells, usually in the lobular zone. Clinically also there are marked differences; for example, a high ammonia coefficient is of good import in eclampsia. It augurs ill in the liver necrosis. The urine in the former contains albumin and casts. In the latter there are few or no casts and little or no albumin. The vomiting of pregnancy he divides into three groups—reflex, neurotic, and toxemic. Differentiation between the first and second Williams makes by the proportion between nitrogen as ammonia and nitrogen as urea. In the former the ammonia nitrogen is less than 5 per cent. of the total. In the latter it may reach 50 per cent. In a case of vomiting in pregnancy Williams makes his diagnosis of variety largely by this determination. The total nitrogen in toxemic vomiting is not much changed and there is but little albumin in the urine. Perhaps of greater clinical importance is the view of Williams that such routine examination in cases of vomiting can sometimes give information by which the condition may be stopped short of fatal liver necrosis. In the main he agrees with the views of Stone Eddy.[2]

Chloroform Poisoning. Wells[3] believes that the poisoning process in delayed cases of poisoning after chloroform anesthesia is similar to the action of chloroform as seen in experiments outside of the body. That is, synthetic activities are depressed or suspended while autolytic processes continue. Its poisonous action is largely independent of its anesthetic property, which seems to be due to its solvent effect on the lecithin and cholesterin content of the nervous tissues. A period of 10 to 150 hours elapses be-

(1) Am. Jour. Med. Sciences, September, 1906.
(2) Pract. Med. Series, October, 1905.
(3) Jour. Am. Med. Assoc., Feb. 3, 1906.

tween the time of anesthesia and the appearance of the symptoms of poisoning. Chloroform poisoning is common with a number of closely related conditions characterized by intoxication and marked changes in the liver, as in acute yellow atrophy and phosphorus poisoning, depending upon the destruction of the synthetic functions of the organ without the destruction of its autolytic ferments. Autolysis of the liver cells takes place, resulting in changes in the liver structure and the appearance of the products of autolysis in the blood and urine—amido acids and other acids. In chloroform and phosphorus poisoning the oxidizing ferments are probably the disturbed elements, and that may account for the marked fatty changes that are present in these conditions.

The Nature and Pathology of Eclampsia. Parnall[1] says of fatal eclampsia that the characteristic hepatic changes are not present in every case, and when occurring are probably secondary; that the disease is a toxemia which he thinks quite possibly is of placental genesis and that alterations in the thyroid may have a bearing. In one case he found necrosis of the epithelium of the tubes at the distal end of the proximal convolution.

Carefully reviewing the literature and studying the pathology in some cases of eclampsia, he concludes:

1. That eclampsia is due to a toxemia, the origin of which is not known but which in the light of recent investigations is quite possibly of placental origin.
2. Characteristic hepatic changes are not present in every case of the disease, and when occurring are probably secondary.
3. That in rapidly fatal cases the kidneys, as eliminative organs, will probably be first affected by the poison, and will show the chief changes in the epithelium of the distal portion of the proximal convoluted tubules.
4. Alteration in thyroid gland function may be directly or indirectly responsible for the development of the toxemic state resulting in eclampsia.

The Malignancy of Vesicular Mole. Schickele[2] says we have no histologic test for the benignancy or malig-

(1) Am. Jour. Obstet., October, 1906.
(2) Archiv f. Gyn., Bd. LXXVII, Heft. 1; Surgery Gyn. Obst., June, 1906.

nancy of vesicular mole. In recent years we have learned that the formation of vesicles is less important than the proliferation of the chorionic epithelium. This characteristic it has in common with chorioepithelioma, the two differing in the intensity of the proliferation.

The presence of syncytium in the stroma of the villi can not be taken as evidence of the malignancy of a vesicular mole, for such conditions are found in benign moles, and are wanting in moles followed by chorioepithelioma; and even in the normal placenta syncytium has occasionally been seen in the stroma of the villi. The migration of villi in vesicular mole does not justify calling it malignant, nor is it an evidence of malignancy in the mole to have some of these migrated villi undergo malignant degeneration outside the uterus.

When the epithelium of the vesicular mole proliferates and penerates the decidua or the wall of a vein, and burrows into the muscularis, destroying it, the process is malignant. A chorioepithelioma may develop long after the removal of the mole, and is only related to it in that the latter furnished the fetal elements for proliferation.

It is hard, he says, to draw the line between the so-called destructive mole and a chorioepithelioma.

A fatal result is not proof of the malignancy of a vesicular mole.

Concerning the treatment of these cases, the author says every vesicular mole should be regarded as dangerous, and after its removal the uterus should be curetted and the material examined. If an extrauterine chorioepithelioma is found coincident with vesicular mole in the uterus (he mentions four such cases), both should be removed and the uterus curetted. If the findings are negative, exploration and examination should be repeated in four weeks, or earlier if a malignant process is suspected. If the primary or a subsequent curettage shows proliferating epithelial elements with destruction of the musculature, removal of the uterus is justified.

The presence of a chorioepithelioma outside the uterus is not alone a sufficient indication for removal of the uterus, and only becomes so when examination of the uterine scrapings point to the malignant character of the uterine growth.

In the light of our present knowledge, vesicular mole must be regarded as quite rare, and its prognosis not in such a degree bad as to make an absolute indication for immediate extirpation of the uterus.

Development of Extrauterine Decidua. It has been fairly well established that the decidual cell is a modified connective tissue cell, the modification being brought about by the influence of pregnancy. At least two questions are still frequently discussed. Can decidual cells be produced in tissues other than those derived from Müller's tube? Can other stimuli than pregnancy result in decidual cells? Lamborn,[1] studying the first of these questions, concludes that decidual cells can originate at least in the Fallopian tube, and possibly also from the endothelium of the peritoneum, and of blood vessel lining.

As we have no definite means of staining decidua cells so that we may be able to differentiate them from all other cells morphologically similar, and as most of the cells found on the peritoneum and in the ovaries have been described as occurring in clumps, is it not possible that something has been described as decidua that was not decidua at all? Can we take isolated cells, and say positively that they are decidua cells?

Rossi Doria says that, especially in the later stages of development, it is easy to confuse Langhans cells with decidua cells, but still believes it possible to differentiate the two, and gives the following characteristics for each: Langhans cells are small, with a comparatively large nucleus; little, slightly staining protoplasm, and without intercellular substance. Decidua cells, on the contrary, are, in general, much larger, as a result of their large protoplasmic contents, in comparison with which the nucleus is small, notwithstanding it is somewhat larger than that of the Langhans cell. They have, while in small amount, a slight fibrous intercellular substance, and take up less of the stain than the trophoblast cells. All of these differences are not of the nature that they can be seen at first sight, but appear only after a certain amount of study, when one takes into consideration the origin of the two.

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(1) Surg., Gyn. and Obst., September, 1906.

Veit says that cells occur in the serotina which one may question whether to class as Langhans or real decidua cells, and that he can readily understand how, when one sees places where there are no decidua cells, he comes to the conclusion that there is no decidua present, and that the cells there cannot be decidua cells. The question of the border-line between the fetal and maternal tissues belongs to the most difficult in the anatomy of the placenta. He says, further, that to draw the line between fetal and maternal tissue from the cells alone is practically impossible.

The similarity of lutein cells and decidua cells has been so often pointed out that it scarcely needs to be mentioned here. The writer has had no chance to study any of the cases of decidua in the ovary, so he cannot say anything of them. Webster believes that he can differentiate between the two.

Ries has shown specimens of proliferated endothelial cells in the tube and about the appendix. These showed well the difficulty one has in trying to diagnose decidua cells from the cell alone. In these cases pregnancy was excluded and Ries was able to trace the origin of the cells to the endothelium of the peritoneum; yet von Franqué could well have used one of these specimens in making his drawing of a pseudoglomerulus with decidua cells. The fact that adhesions were present in most of the cases where decidua was described on the peritoneum is a point which seems to speak very strongly for the possibility of a confusion of proliferated endothelium and decidua. The case was one of tubal pregnancy at about the tenth week.

The gross specimen was a part of the left Fallopian tube with a dilatation about the size of a hen's egg. The dilatation extended to within a centimeter of the fimbria, and the tube was amputated close up to the other side of it.

The external surface of the sac showed some signs of adhesions, but otherwise nothing of special interest. The wall had a rupture in its dorso-lateral part, and from this opening projected tufts of chorionic villi. Within the sac was found a fetus, about 6 c.m. in length, and a well-formed placenta. The placenta was attached to the inner surface of the sac wall adjacent to the broad ligament, and

covered somewhat more of the posterior than of the anterior surface. The rupture was seen to be near the lateral margin of the placenta, but still within the placental site, as is the rule in these cases.

The sac wall varied much in thickness. In places it was infiltrated with coagulated blood and measured as much as a centimeter. At the placental site it was thinnest, measuring in places not more than one-half of a millimeter in thickness. The inner surface at this point contained elevations in the form of folds varying in height from a half to two millimeters or more. Lying close against the inner surface of the wall were the chorionic villi, making up the placenta, which was about a centimeter thick.

The sections, except one, came from the placental site, and were stained with hæmatoxylin and eosin.

Microscopically, the sac wall is made up of a fibrous stroma with involuntary muscles and blood-vessels. The muscle tissue in places is much less than the amount found normally in the tube wall, and is not so definitely arranged in layers. It also has the appearance of being somewhat degenerated. The blood-vessels vary much in size and appearance. Some are large sinuses with only an endothelial wall; others are small, with a thick wall, and correspond to arteries; while still others, of various sizes, are surrounded by and more or less filled with cells which seemed to have either infiltrated or replaced their walls.

The connective tissue stroma of the sac wall, especially near its inner surface, is infiltrated with large, round, oval, or polygonal cells. The protoplasm of these cells varied from a darkly stained, coarse granular to a transparent vascular. The nucleus is vesicular, comparatively poor in chromatin, and usually contains one or more nucleoli. These cells resemble very closely some of those surrounding some of the vessels. The cells do not lie closely, but have more or less stroma between them. In places one can see that the nearer one comes to the surface, the larger the cells are, and as one goes deeper, they take on more of a spindle shape.

The question is, whether we have here to do with modified connective tissue cells, in other words, decidua cells,

or whether we have the connective tissue of the sac wall infiltrated with fetal (Langhans) cells.

Gebhard, in describing the attachment of the chorionic villi to the serotina in the uterus, says that those of the villi which come in contact show on their point a marked development of the Langhans cells which are arranged in cell columns and break through their surrounding of syncytium and become so completely united with the decidua that it is not possible to differentiate the fetal from the maternal tissue.

One specimen shows that very nicely. We have the Langhans cells extending beyond the end of the villus, becoming more and more spindle shaped and farther apart. Farther on we have cells more nearly round, and, finally, cells like those described before as filling the connective tissue of the sac wall. One has a gradual gradation between the Langhans cells adjoining the villus and the cells within the sac wall. This is undoubtedly what Tassenbroek saw and described as a decidua fetalis made up of maternal tissue infiltrated with Langhans cells. As a matter of fact, it has never been proven that the Langhans cells infiltrate the maternal tissue except along the blood vessels, or when we have to do with a malignant growth, as in the chorioepithelioma. Veit, while he believes that the trophoblast may grow into the maternal veins and become completely detached from the chorionic villi, rejects the idea of the Langhans cells entering the connective tissue of the mother. Furthermore, if these cells were Langhans cells which had grown into the maternal tissues, it seems strange that they should be so evenly distributed. It is much easier to explain them as originating from the connective-tissue of the sac wall, and then the smaller cells which lie more deeply, and often show a spindle or stellate character, would answer well Marchand's description of the young decidua cell. It might further be stated that a certain number of observers, who believe that decidua is developed in the tube, have doubted the development of a decidua serotina, and it has seemed strange that only certain parts of the sac wall should develop decidua. It seems more probable that they have looked upon decidua cells as Langhans cells.

While syncytium is unmistakably to be seen at places

in the lumen, certain of the cells in the walls of blood-vessels resemble very closely decidua cells. That the vessels which are surrounded with these cells are arteries, as was found in Fellner's cases, does not seem certain. However, some of them may be, and indeed some of them appear to be. That all of the cells should be fetal in origin does not seem probable, and the writer maintains that there is some good reasons for believing, as Fellner and Cornil do, that the vessel wall may show a decidual transformation.

The other specimen did not come from the placental site. It shows on its peritoneal surface signs of inflammation and a proliferation of endothelial cells resembling closely decidua cells. That these are not true decidua cells seems evident. However, if they had developed to a somewhat greater extent, and penetrated somewhat deeper into the tube wall, so that one could no longer show their relation to the surface, they could possibly have led to an error. Yet these masses can usually, in serial sections, be shown to connect with the surface endothelium, as Ries demonstrates.

The discussion of Lamborn's paper considered both the first question, to wit, can any other structure than the uterus produce endothelial cells? and also the second question, namely, can anything else than pregnancy produce decidual cells? Part of the interesting discussion is here reproduced:

Dr. Emil Ries: "I had the good fortune of being permitted to look over these sections, and they illustrate the difficulty of differentiating between the Langhans layer and the decidual cells and proliferated peritoneal epithelium.

"Of course, as long as the questionable cells are inside the tube there is no difficulty in excluding the origin of these cells from peritoneal epithelium, but when the tissue comes from near the peritoneum, the difficulty is greater.

"I examined a specimen which I removed from a girl of 16, who had occlusion of the hymen, hematocolpos, hematomata, and hematosalpinx. The girl, of course, had never been pregnant. I opened up the tubes, let out the blood, made new openings in the tubes and seamed them, and the tissue that I removed in making the opening I

subjected to microscopic examination. There were areas in those specimens that looked very much like decidua, resembling specimens I saw in Berlin last year in Pick's laboratory. In some places it would be very hard to tell the difference.

"The development of peritoneal growths was thought at one time to be dependent on the presence of pregnancy. But my case proves that the condition does not depend on pregnancy; that it may occur in other conditions. In fact, I believe that it depends only on irritation of the peritoneum. The cases of extrauterine pregnancy operated on usually are not cases with a normal peritoneum. There has been some hemorrhage, some rupture, some distention of the tube, and irritation. I have examined some specimens carefully, and have always found fibrin or some new-formed adhesions, and in these cases the epithelial growths develop most beautifully."

Dr. Charles E. Paddock: "The remarks of the last speaker emphasize the statement I made at a previous meeting, that a diagnosis of ectopic gestation cannot be made because of decidua cells in the discharge from the uterine canal. The case under discussion at that time was one wherein a failure to diagnose an ectopic pregnancy had been made, and the uterus curetted, and scrapings showed decidua cells. This, I claimed, did not make the diagnosis of pregnancy absolute, although the patient was operated upon later, following a tubal abortion. If we expect to make a diagnosis of tubal pregnancy because of the finding of decidua cells in every case, we will occasionally be mistaken. There must be found distinct fetal tissue, and until we do find this it is not safe to diagnose tubal pregnancy."

Dr. George E. Schmauch: "I agree with Dr. Ries and also with Dr. Lamborn. The most important statement I have heard made so far is, that we are not able to say this is a decidula cell, and this not. The individual decidua cell has no characteristics. The doctor started his investigations assuming that the decidua cells always originate from connective tissue. If we assume that, there is no use arguing about these things. Every connective tissue cell undergoing changes such as those met with in pregnancy and other conditions certainly cannot be called

a decidua cell. The enlarged connective tissue cell assumes, as we say, an epitheloid character, as, for instance, in tuberculosis, in the endometritis interstitialis. These cells have the same appearance as decidua cells. They are decidualistic cells.

"In my opinion, there is no decidua formed in the tube. The real decidua—a continuous membrane—is formed only in the uterus, and this mucosa is not the same tissue as that we find in the tube. The characteristics of the uterine decidua is to be seen in an exceedingly fine reticulum, and in its meshes the decidua cells are lying.

"The doctor spoke about mistaking Langhans cells for decidua cells. That is not possible. By Langhans cells we mean a well-defined cell. He probably means trophoblast cells invading the fetal tissue. We have different means of distinguishing between different cells, as the structure of the cytoplasm and nucleus, their affinity to stains, also their surroundings. The connective tissue and the epithelial cells are very characteristic. Krompechner's researches, however, show that the difference between the two is not as great as was thought. The same observation is made when we examine cases of early pregnancy, especially tubal pregnancy. We are not always able to differentiate the invading trophoblast—an epithelial cell—from the surrounding connective tissue cell.

"There is another group of cells which may be confused, and these are the so-called plasma cells, also maternal cells, which are always present in tubal pregnancy. There are two things by which I determine fetal and maternal cells. Decidual cells may be recognized by the reticulum surrounding the decidua cells, and the fetal cells are recognized by the destruction which the connective tissue around the cells undergoes. We regard the connective tissue as an intercellular substance pervaded by channels, and in these channels protoplasmatic lumps, the connective tissue cells, are lying. Fetal cells may invade these channels, and the connective tissue cell itself may assume an epitheloid or decidua-like character. The result, however, never will be a continuous decidua. The picture these enlarged cells present will vary according to the prevalence of the intercellular substance of the tissue. At times only a few large cells are scattered through the tissue

around the villi, and at other times the cells are lying close together.

"Other specimens show blood-vessel walls made up of large cells which resemble completely decidua cells. The intercellular substance between these cells is normally scanty, consequently the likeness to decidua cells. All those decidua-like cells which we find in the peritoneum during pregnancy are, in my opinion, always situated around the lumen of the vessel, and are perivascular cells that have undergone an epitheloid change."

Dr. Lamborn (closing the discussion): "With regard to Dr. Schmauch's question as to the trophoblast and Langhans cell, I understand by the latter a cell that is developed from the syncytium, whether inside or outside of the latter does not make any difference, as they may break through the syncytium later.

"That the hemorrhage of tubal pregnancy is due to cytolytic action of the trophoderm is the opinion of Goffe.[1] The trophoderm is ectodermic in origin. They are of large size. They produce destruction of the adjacent walls. This destruction may carry on the walls of vessels of some importance. Invading the walls of the vessels, they cause hemorrhage."

Breuss Hematomole. A study of a Breuss hematomole is reported by Brill.[2] The essential peculiarity of this mole is a disproportion between the size of the embryo and that of the ovum. The embryo is usually of the degree of development that is found at four to six weeks. A placenta is definitely formed, though acharacteristic in many particulars.

Tuberous lobulated hematomata, too, are found in the chorion. The vessels of the villi are poorly developed. The cells of Langerhans and the epithelium of the chorionic villi are particularly ill developed. Trophoblasts persist. Everything goes to indicate that just as the connection between the embryonic and maternal blood-vessels were made the embryo had died. There had been enough contact growth to permit of some growth in chorionic and placental structures. The fetal mass had undergone but little

(1) Jour. Am. Med. Assoc., Nov. 4, 1905.
(2) Am. Jour. Med. Sc., July, 1906.

retrogressive changes. No case of infection of the partially dead mass has been reported.

Bacteriology of Cystitis in the Female. Taussig,[1] studying this question, found the normal uretha sterile in 14 per cent. of the cases. In 62 per cent. of the urethas which he examined pathogenic bacteria were present. The most frequent organism was staphylococcus. Colon bacillus was seldom present except in those cases which were confined to the bed.

Carcinoma of the Cervix Uteri. Sampson[2] found carcinoma of the cervix to be of three types—adenocarcinoma, infrequent but quite malignant; the cauliflower type of squamous cell carcinoma, the least malignant of the three. The investing or ulcerative type was the most frequent. It was quite malignant. The carcinoma spread directly to the parametrium by metastasis to the lymph nodes of the parametrium and to the pelvic lymph nodes. The malignancy of adenocarcinoma of the cervix demonstrates that the degree of malignancy of a carcinoma is dependent more upon its location than upon its histologic type. In the series of 27 cases the parametrium was found infected in 17. The pelvic lymph glands, in the opinion of Sampson, are infected in one-third to one-half of the cases of operable carcinoma.

Cystic Aplasia of the Cerebral Hemispheres. Bullard and Southard[3] describe the autopsy findings in an idiot dying, at 37 months, of broncho-pneumonia. The child had been subject to convulsions after its twentieth month. At the autopsy very little thymus tissue was found. The cerebellum was normally developed. In the cerebrum were very large loculated cysts with some reticulum spanning the cavity. The pial spaces did not communicate, nor did the lateral ventricles. Special staining demonstrated that the ependymal cells did not line the cysts. The cyst lining was not of the same nature as the pial structures. There was little evidence of gliosis. The authors conclude that the trabeculæ were remnants of neuroglia tissue. The injury was to the nerve elements proper, and caused degeneration of these, or lack of development, and at the

(1) Am. Jour. Obstet., October, 1906.
(2) Am. Jour. Obstet., October, 1906.
(3) Jour. Med. Research, January, 1906.

same time allowed the neuroglia elements to develop. The outside brain form was negative except for some deficiency of convolutions.

Ankylosis. Murphy[1] says that embryologically the bone, cartilage, capsule ligament and periarticular fibrous tissue are closely related. Heredity is responsible for the location of joints and for their primary anatomy; yet function is responsible for their fuller development and continuance of usefulness. The close relationship of these different structures makes it easy to convert any one into any other. Fibrous tissue readily becomes cartilage, and cartilage readily becomes bone. Therefore if the function of the joint for a time is interfered with, such a change of tissue from the one kind to another is always liable to occur. Just as we know that the endothelium of the blood vessels can easily be converted into ordinary fibrous tissue, so the cellular covering of the joint surfaces is not specific. It serves to prevent union largely because of the use to which it is put. It may very readily assist in firmly joining together by organic union the two bones entering into the joint or any other structures round about. While this has been fairly well accepted for some time, the converse proposition advanced by Murphy has not been as generally known. It is that the neighboring connective tissue can be used for lining artificial joints and that it will take on the needed cell characteristics if the joint is kept in use. Murphy thinks that a good deal of adipose tissue must be included in the inserted tissue. He lays stress upon the conversion of the adipose into a hygroma by the liquefaction of collagen. [We are of the opinion that there is nothing specific in this liquefaction. Adipose tissue is advantageous because it is a loose tissue with fibers running in no particular direction. The fat globules are readily dissolved and disappear, and the connective tissue becomes looser still. For these reasons the interposed fibrous tissue is spared the destructive effects of primary and secondary tension. Other than this the idea is sound, and the principle should be productive of good in more than one direction.—Ed.]

(1) Jour. Am. Med. Assoc., May 20, 1905.

SECTION IV.

BACTERIOLOGY.

CHEMISTRY OF THE BACTERIA.

Endotoxins. Soluble endotoxins of typhoid plague and dysentery bacilli are obtained by Besredka[1] by the following method: The bacteria are scraped from young agar cultures, suspended in physiologic salt solution and heated for one hour at 60° C.; after this the suspension is dried in a vacuum. Dry sodium chlorid is mixed with the residue and triturated for an hour; water is now gradually added during the rubbing procedure until an equivalent to make a physiologic solution again. If it is the typhoid bacillus that is under preparation the solution is heated a second time on the water bath for an hour; it is then allowed to stand for ten to twelve hours, when the supernatant liquid is withdrawn and contains the endotoxin. When plague or dysentery bacilli are used the suspensions are centrifuged to separate the bacilli, because their endotoxins are injured by heat.

The three toxins showed different points of thermic destructibility. That for typhoid was found to be 127° C.; for dysentery, 80° C., and for plague, 70° C. This is so characteristic that the writer considers it a possible method of recognizing different endotoxins.

Bacterial Autotoxins. H. Conradi and O. Kurpjuweit[2] have made extensive cultural experiments with *Bacillus coli,* from which it results that during their growth the

(1) Ann. de l'Inst. Pasteur, April 25, 1906.
(2) Muenchen. med. Woch., No. 32, Sept. 12, 1905.

bacilli develop inhibitory substances which check not only their own growth but that of all other bacteria of the coli type, such as bacilli of the typhus and paratyphus as well.

Loeffler's bouillon was used as culture medium, this being found best adapted for the solution of the bacterial autotoxins. The growth-impeding activity was evident after the first hour of development, and it increased from hour to hour until it reached its maximum in 24 hours. This antiseptic power persisted for a few days and then disappeared gradually from the culture in from 6 to 14 days. The observations were carried on solely on plate agar cultures, as the bouillon cultures are not adapted for such experiments.

The writers noted further that a direct relationship exists between the growth of bacteria and the rate at which their autotoxins are produced. The greater the growth, the stronger also the growth-checking properties of the culture.

The writers have continued their cultural experiments with colon bacilli on bouillon cultures diluted with physiologic salt solution or bouillon, and the antiseptics produced by the growth of the micro-organisms were found to be more powerful than carbolic acid in impeding the growth of typhus, paratyphus, and colon bacilli. R. Koch has shown that the growth of bacteria is impeded by carbolic acid in a solution of 1/1250 and is checked by a solution of 1/850; but the writers found that a solution of 1/3200 of the bouillon, on which the bacilli had grown, is sufficient to show distinct growth-impeding properties. The culture, however, showed only growth-impeding properties, and no antiseptic or bactericidal activity. The antiseptic properties of the cultures are destroyed by heat (boiling temperature). Filtration through Berkefeld filters renders the bouillon inert. Other means were employed with a view to separate the antiseptic substances from the bodies of the bacteria, but without success. The separation of the autotoxins was finally accomplished by means of dyalisis.

Antibodies. *The Question of Ferments in Immune Bodies and Complements.* Liebermann,[1] who found a negative answer to this proposition after experiments with

(1) Deutsche med. Wochens., Feb. 15, 1906.

toxins, reaches a similar conclusion for amboceptor and complement. This writer formerly held the view that ferment action was the basis of these phenomena, but now finds it necessary to reverse his opinions.

In order that a ferment should be recognized the specific action must be repeated without reaching any very definite limit of activity. That is, the quantity of ferment itself that is present has very little to do with the results observed. This is not the case when experiments in hemolysis are closely observed. The results here as shown by the laking of the corpuscles will bear some relation to the amounts of immune serum and complementary serum that have been used. Several experiments are presented to illustrate this point. Rabbits were immunized against pig corpuscles by receiving a number of injections of washed pig corpuscles and later the immune serum was withdrawn from the rabbit's ear. Mixtures were made as shown in the following table and these were placed in the incubator to give opportunity for the hemolytic action to take place:

	Drops.			
	1.	2.	3.	4.
Emulsion of pig corpuscles.....	40	40	40	40
Inactivated immune serum.....	4	4	4	4
Normal pig serum.....	8	16	32	64
Physiologic salt sol.....	28	24	16	0
Total	108	108	108	108

Upon taking the tubes holding these mixtures from the incubator each was centrifuged and the clear supernatant liquid showed:

1. Slight redness.
2. Darker red.

3 and 4. Much darker red but no great difference.

The results were in proportion in a general way to the amounts of immune serum that was added, but a limit apparently had been reached in Nos. 3 and 4.

Another series of tests in which the amount of immune serum is gradually increased is presented:

	Drops.			
	1.	2.	3.	4.
Emulsion of pig corpuscles.....	40	40	40	40
Normal pig serum.....	4	4	4	4
Inactivated immune serum.....	4	8	16	32
Physiologic salt sol.....	28	24	16	0
Total	76	76	76	76

Here the results were seen when the tubes were again taken from the incubator and centrifuged:

1. Decided redness.
2. Darker red.
3 and 4. Still darker red.

It would appear from this that the complement had been used in each instance and showed nothing of a ferment action.

This is not simply a subject for speculation, but has in it much that is practical. If the antibodies are ferments, for example, it would be of lesser importance to determine the quantities required to achieve immunity in practice than to know the conditions that would continue the ferment action or modify it. If they are not ferments, then experimental determination of quantities is of utmost importance, and also the necessity of supplying the maximum amount of complement must be held in mind.

Detachable Agglutinogen. Following previous experiments in which it was shown that the agglutinability of typhoid bacilli was greatly reduced when the cultures were heated Bixton and Torry[1] have added new facts to this interesting subject. When an emulsion of typhoid bacilli is heated to 70° C. and filtered through a porcelain filter a part of the agglutinin passes through the filter and may be found in the filtrate. These have been called free receptors, or by some, as Rossi (Centr. f. Bakt., Vol. xxxvii, 1904, p. 433) detached flagilla. The immunization of animals with tests of the immune sera produced by using filtrates and washed bacilli are described by the writers.

(1) Jour. Med. Research, April, 1906.

Stable agglutinin is that part that remains with the bacilli, and detachable agglutinin is that portion that appears in the filtrates following the stripping of the bacilli. Upon injecting rabbits with these two materials it was found that the filtrates containing detachable agglutinin were more toxic than the bacilli. The value of the two sera obtained is shown in the following table:

		Serum Dilution, one to					Time
Serum	Emulsion of	100	1000	10,000	20,000	50,000	
Bacillus	Typhoid Bac.	+ +	+	--	—	—	3 hours
Filtrate	"	+ + +	+ + +	+ +	+	—	

This table shows that the bacillus serum agglutinates typhoid bacilli very slowly, and it was further seen that the clumps are small and compact. This is the way heated bacilli react when treated with ordinary serum.

Filtrate serum agglutinated normal bacilli very readily and in high dilutions the clumps were large and flocculent. It was further found that the bacillus serum agglutinates stripped, while the filtrate serum does not except in low dilution. It may be concluded that the agglutinogen of the typhoid bacillus is not a single substance; it may be divided into a stable and a detachable agglutinogen, which may be separated mechanically or by heating to 70° C. The injection of these two parts develop in animals sera showing different properties, as regards their activities in causing agglutination of the bacilli.

Complements. The question of the multiplicity of complements in bacteriolytic sera has been studied by Foster,[1] who decides that normal goat's serum contains only one complement for cholera and typhoid fever. The union between organism, amboceptor and complement is probably dependent on degrees of concentration of the mixtures, and also upon the length of time during which it occurs. The serum in contact with the clot is comparable with human serum in its bactericidal action on typhoid and cholera. When normal goat serum is saturated with sterilized typhoid bacilli the dead bacilli are capable of remov-

(1) Lancet, London, Nov. 25, 1905.

ing the complement for both typhoid and cholera. Diversion of the complement in normal serum may be induced by the addition of the same serum heated.

Auxilytic Serum. The terms auxihemolysin and auxihemagglutin are applied by Manwaring[1] to bodies capable of increasing hemolytic and agglutinating activities, respectively, in immune sera. If normal goat serum is heated to 56° C. for 30 minutes it loses completely its power to reactivate a hemolytic goat serum rendered inactive by heat. The complement originally present in the serum is completely destroyed by such heating. If the heating is continued for three or four hours the serum undergoes further changes and acquires the new property of being able to enormously increase the action of a hemolytic serum to which it is added. If heated still longer this property is lost. Under this treatment the agglutinating properties are preserved longer than the hemolytic properties.

Antibodies, Passage to the Young. Some additional information as to the fate of antibodies when injested by nursing infants is brought forward by F. la Torre.[2] Are these bodies absorbed in any useful quantities into the blood itself? The experiments presented were on the nurses and nurslings in seventeen cases. In five cases the wet nurse was injected with 3,000 units diphtheria antitoxin, and for each of the other twelve nurses 6,000 units were used. This amount of serum was given in divided doses. The antitoxic power of the children's blood was tested the day before the injection of the nurse and again three days after the injections. This serum test was made by mixing one or more minimal lethal doses of diphtheria toxin with serum from the child's blood. Guinea-pigs were injected with the mixture. The results indicate that the antitoxin power present is very slight. By calculation the writer estimates that no more than one thousandth part of the antitoxin given the wet nurse reaches the child's blood. Such passage as was demonstrated does not depend upon the age of the children.

Biologic Blood Test. Neisser and Sachs[3] have adopted

(1) Central. f. Bakt., I Abt., Orig., Bd. XLII, No. 1, 1906.
(2) Ill. Policlin., December, 1905.
(3) Berl. klin. Woch., Jan. 15, 1906.

a method of checking the results of the Wasserman method of testing for human blood for forensic purposes. The principle in the tests is that antihemolysins occur in antisera. Rabbit serum has a normal hemolytic action for sheep corpuscles. In following out the test a sufficient quantity of rabbit serum is taken so as to completely lake the amount of corpuscles used in the experiment and a solution of the suspected human blood as well as a quantity of antihuman serum are mixed with it. The mixture remains in the ice box for one hour and there is then added the suspension of sheep corpuscles. If the suspected material contains human blood this reacts with the antiserum and the rabbit serum is thus free to cause the laking of the sheep corpuscles. In the case of a negative result the antiserum is not disturbed and consequently exerts its antihemolytic action and prevents the laking of the sheep corpuscles by the rabbit serum. The test is said to be positive to the presence of .00001 c.c. of human blood. It was used with success in connection with two medico-legal cases.

Locle[1] recommends an alkaline formalin serum mixture for the injection of animals in preparing the biologic blood test. A mixture consisting of distilled water, 75 parts; calcium chlorid, 1 per cent. solution, 15 parts; magnesium chlorid, 1 per cent. solution, 10 parts, and formalin, 1 part, is added to an equal quantity of the serum or tissue extract to be used. Decomposition is avoided by this method and the writer found that the precipitation tests that he made were unusually clear.

Phagocytosis. Bergey[2] finds from his studies on phagocytosis that under opsonic stimulation the macrophages take up more bacteria than the microphages. The figures in his counts are:

	Microphages.	Macrophages.
Bact. pseudodipht	1.46	4.86
Streptoc. pyog., urine.....	3.45	7.91
Streptoc. pyog., scarlet fever...	3.91	6.78
Mic. pyog. albus.....	2.17	3.41
Mic. pyog. aureus.....	3.30	8.29
Mic. catarrhalis	3.90	4.51

(1) Muench med. Woch., No. 22, 1906.
(2) Jour. Am. Med. Assoc., Aug. 25, 1906.

The results also indicate that the opsonic power of the blood serum is more pronounced for those bacteria which induce septicemia than for those against which there is a more distinct bacterial immunity.

Clemens[1] explains the opsonic index of Wright in a very clear description:

"If, from the blood of a patient, which has shown under the microscope active phagocytic action in the presence of bacteria, the blood serum be taken and kept at a temperature of 60° C. for fifteen minutes, it will be found on mixing this blood serum with equal quantities of washed leucocytes and bacteria that all phagocytic action on the part of the leucocytes ceases. Wright has made use of this observation as a means of comparing the resistance values of different blood sera in the following manner: If the leucocytes in the blood serum of a healthy man ingest on an average 5 bacteria per leucocyte, and if the leucocytes in the blood serum of a patient ingest on an average 4 bacteria per leucocyte, then the opsonin value of the patient's blood serum, expressed in terms of the healthy man's opsonin value (taken as unit), would be 0.8,

$$\text{for } 5:4::1:x, \text{ or } x=0.8.$$

"This value (0.8) Wright calls the *opsonic index* of the patient's blood serum.

"From this determination to its practical application as regards the study of bacterial inoculation (especially with tuberculin) was but a step. By taking a series of opsonic indices of a patient's blood who had been vaccinated with tuberculin, Wright found that immediately after the inoculation (and for some time afterward) the opsonic indices steadily fell ("negative phase") so that if the opsonic index at the time of inoculation was 1, the indices steadily fell to 0.6, 0.4, 0.2. Then the indices began to show a series of upward values, 0.4, 0.6, 0.8, 1, 1.2, 1.4. This phenomenon Wright calls the 'law of ebb (negative phase), flow, reflow, and high tide of immunity.' The accompanying chart shows these points well."

As a preliminary step to their studies of opsonins

(1) St. Louis Med. Rev., Feb. 3, 1906.

McFarland and L'Engle[1] report experiments upon the phagocytic power of normal blood. The experiments required the bringing together of living phagocytes with the bacteria they were to take up under invariable conditions. First, in order to obtain the cells in proper condition the generally known method of using a 1 per cent. sodium citrate solution in physiologic salt solution was

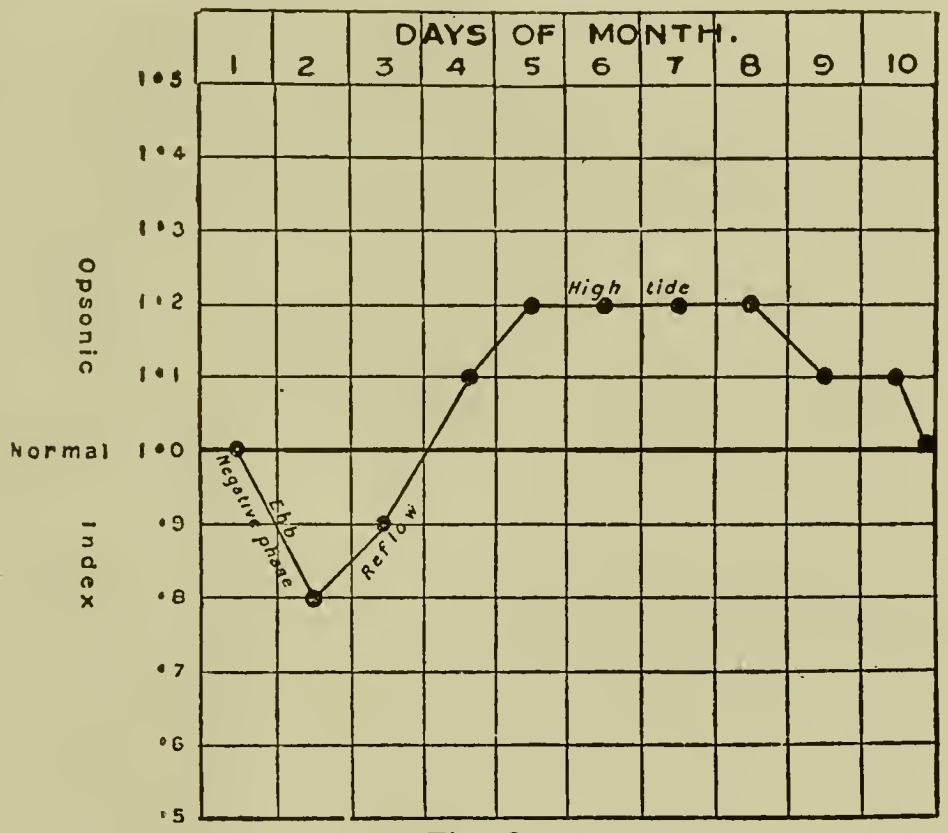

Fig. 3.

used. It is done as follows: The solution mentioned above is drawn into a pipette and then an equal quantity of blood from a thumb puncture is drawn in after it. Both are blown into a watch crystal and mixed. Next, the matter of uniform bacterial suspensions had to be considered. For this purpose the writers devised a standard which they have named the "nephelometer." In previous experiments the bacteria had been actually counted, but in this the nephelometer shows the result by a comparison of turbidity. The turbidity standards are made by mixing a 1 per cent. solution of barium chlorid with a 1 per cent. solution of sulphuric acid, using from 1 to 10 per cent. of the former. These mixtures were made

(1) Medicine, April, 1906.

in small test tubes and sealed off, so that the precipitates of barium sulphate and the contained liquid remained permanent. The staphylococci used were from 24-hour cultures and were suspended in physiologic salt solution. The turbidity of these was compared with the standards by using the same sized tubes and reading against white light, as shown in Fig. 2. The 5 per cent. barium chlorid was generally found most efficient. The mixture of the bacterial suspension and the citrated blood was made by using a capillary pipette much the same as in preparing the blood. Following is the technique:

The capillary is filled to a mark with suspension and then an equal amount of blood is drawn in; both are expelled to cause mixing and the tube is refilled. These filled tubes are sealed and placed lying down in the incubator for 30 minutes. Films were made and stained by the Maringo method. This stain consists of:

No. 1.

Methyl blue	.5
Azur II	.5
Water	100.

No. 2.

Sodium carbonate	.5
Water	100.

The solutions are mixed and placed in the incubator for 48 hours. A 2 per cent. solution of eosin in water is added

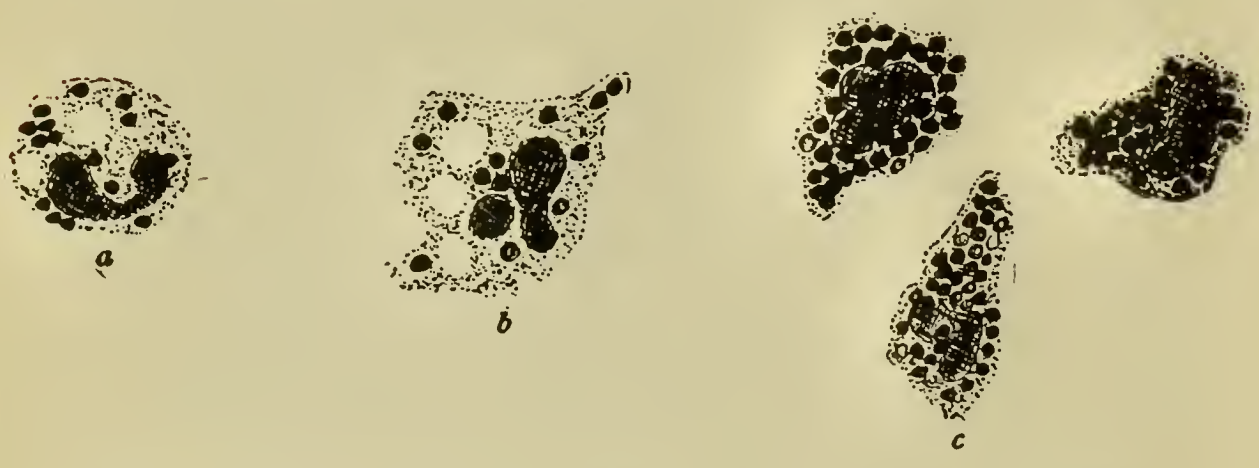

Fig. 4. Leucocytes containing staphylococci *a* and *b* after 30 minutes' exposure, *c* after 60 minutes' exposure, according to the method described, at 37° C.

and the fluid is filtered. The residue on the paper is dried and dissolved in wood alcohol in 2 per cent. strength. In counting the bacteria taken up by the cells the writers count the number of bacteria in each of the first twenty cells observed and take the average count. The tabulated findings for the blood of healthy persons examined showed a variation of 23.2 to 4.125 as the extremes. There is no uniformity in the opsonic index of normal blood. In the same person it may vary according to health. In making studies along these lines the only standard for comparison that can be taken is the patients' own blood. See Fig. 4.

The Aggressivity of Pathogenic Bacteria. Of all the known bacteria but few are pathogenic, that is, capable of multiplying in the animal body and thereby causing disease. The fact that the pathogenic power of such bacteria may be increased or decreased by artificial means indicates that their pathogenicity depends on something more than their "racial characteristics," whatever that may mean.

Oskar Bail[1] discusses in a very interesting paper the power of the pathogenic micro-organisms to conquer the defensive powers of a normal, healthy animal organism, and inquires into the nature of their specific aggressivity. He reviews the work so far done with a view to obtain the aggressive principles of bacteria, and enumerates as follows the properties of an aggressive fluid, such as peritoneal exudate obtained from an animal inoculated with deadly doses of pathogenic bacteria: 1. Such fluid, when cleared of bacteria by centrifugation and proper sterilization, will render deadly quantities of the respective bacteria, otherwise insufficient to cause death. 2. When injected simultaneously with a simple deadly dose of the respective bacteria, it will not only hasten death, but post-mortem examination will also reveal an extensive infection where the bacteria alone would show a light infection and a scarcity of leucocytes in the peritoneal cavity.

These facts have been proven, as was to be expected, since they are implied in the nature of aggressins; but the following unexpected facts also have been disclosed in connection with the work on aggressins: 1. The simul-

(1) Wien. klin.-therap. Woch., No. 37, Sept. 10, 1905.

taneous injection of aggressin and bacilli increases the efficiency of the bacteriolytic immune serum. 2. Preventive treatment of animals with aggressin, free of bacteria, renders the animals capable of withstanding infection with the respective micro-organism.

The Nature of Complements. When R. Pfeiffer[1] discovered that the bacilli of cholera are decomposed in the peritoneal cavity of immunized guinea-pigs, he also established the fact that the active principles that cause their solution are of the nature of a ferment. The nature of complements has been further clarified through experiments in hemolysis by Bordet, who was the first to demonstrate the formation of immune bodies and complements by the hemolysis of red blood corpuscles with a specific hemolytic immune serum, Ehrlich and Morgenroth,[2] who showed that the complement is affected by heat at 56° C., and others.

H. Lüdke[3] has made a number of experiments with a view to ascertain more closely the behavior and nature of complements. He found that the complements diminished in some cases where normal rabbits were allowed to go without food for some time, and remained uninfluenced in others, so that the results of starvation upon the formation of complements are not always similar. The disappearance of complements as the result of abscess formation was first noted by Métalnikoff, and the writer verified this fact by obtaining two positive results among a large number of immunization experiments upon animals which presented abscess formations as the result of subcutaneous injection of blood. Injections of pilocarpin were found to raise the quantity of complements.

The writer has also made extensive clinical observations. In eleven cases of advanced phthisis the complements were not found to be appreciably influenced. This observation corroborates the results obtained by Keutzler,[4] who found no quantitative difference in the complements of the serum of normal persons and those of 37 patients with tuberculosis which he examined.

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(1) Deutsche med. Woch., 1896, No. 7-8.
(2) Ehrlich, Gesammelte Arbeiten zur Immunitätsforschung, Berlin, 1904, Hirschwald.
(3) Muenchener med. Woch., No. 43, Oct. 24, 1906.
(4) Berlin. klin. Woch., 1904, No. 11.

The influence of the uremic state upon the formation of complements has been studied by several writers, but their results are highly contradictory. Lüdke has had opportunity to make careful observations in four cases of typical uremia. In one, the hemolysis was markedly diminished whether the serum was used pure or with the addition of inactivated serum; in the second the blood corpuscles of the blood of rabbits were promptly dissolved by the active serum, although the action was much impaired by the addition of inactivated uremia serum; in the two other cases hemolysis by the uremia serum failed altogether to take place.

The Multiplicity of Complements in Serum. That there are several varieties of complements has long been known, and Lüdke endeavored to separate each by means of filtration. The normal sera of man and chicken were used for this purpose, and after filtration and exposure to 49° C. he succeeded in separating the complements for the blood of different animals used in his experiments.

Aggressins. Doerr[1] finds, as a result of his experiments, that the recognition of a special body having negative chemiotactic and infection facilitating substances in the sterile peritoneal fluid is not a demonstrable entity. Such fluids, even when perfectly clear, contain bacterial substances, as can be shown by precipitin tests, and the presence of these substances explains, to a sufficient degree, the immunity that results after the injection of the fluids. As the "aggressive" fluids are in themselves poisonous and can cause death of guinea-pigs when injected intraperitoneally, Doerr concludes that there is a depressing effect and a lessened resistance on the part of the host. When very small doses of bacterial toxins, as diphtheria, cholera, are used the character of the infection may be so modified as to give all the characteristics found in those cases where the Bail aggressin has been injected. The fact of a negative chemiotaxis does not explain the unusual severity of such infections, because there is no parallel between the suppression of phagocytosis and aggressin activity. In relation to the half parasites aggressive immunity does

(1) Centr. f. Bakt., Erste Abt., Orig., Sept. 18, 1906.

not differ from that obtained by using dead bacteria or bacterial extracts.

Citron[1] concludes that aggressins are bacterial extracts and that antiaggressins are sera having the same properties as immune sera produced by bacterial injections. The infection acceleration by these bodies is due to their combining power with the normal protective body agents. This includes also the leucocytes. That aggressins can destroy the activity of immune sera is due to the combining of the receptors and disturbance of complement within the body.

The action of subtilis aggressin in the prevention of phagocytosis has been studied by Weil and Nakayama.[2] They found that subtilis aggressin is capable of preventing phagocytosis of the hay bacillus by guinea-pig leucocytes in the test tube. This depressive influence is not due to the hay bacillus extract or guinea-pig serum in which hay bacilli had been grown.

It is probably due to the fact that the aggressin in connection with the bacilli damages the leucocytes. This action is specific.

Action of Aggressins on Streptococcus Pyogenes. Weil[3] prepared aggressin as follows: He injected rabbits, intrapleurally, with streptococci, and after the infection he obtained 15 to 30 c.c. of bloody fluid rich in streptococci and cells. This exudate was centrifuged and the clear fluid was used. Tests as to sterility were made by cultures. Aggressins must cause increased susceptibility and also the production of an antiaggressin. Guinea-pigs were used in the demonstration.

Upon experimentally immunizing guinea-pigs with this aggressin fluid he found that the antiaggressin produced was of very low value, at most only capable of extending the time for the final fatal termination. This action was due to a restraint in the multiplication of the streptococci rather than to any marked variation in the action or relation of the leucocytes in the experiment.

Leucotoxin. Curschmann and Gaupp[4] have investigated

(1) Centr. f. Bakt., Originale, May 17, 1906.
(2) Deutsche med. Wochensch., Jan. 15, 1906.
(3) Deutsche med. Woch., March 8, 1906.
(4) Muench. med. Woch., Dec. 12, 1905.

the condition of the blood of leukemic patients after x-ray treatment as to the presence of leucotoxic substances. It was shown that x-ray treatment accompanied by a leucocyte destruction leads to the formation of leucotoxic bodies in the circulating blood. Such sera are capable of an elective destructive action upon leucocytes in the body of experiment animals and upon human leucocytes when applied in vitro. Such a serum loses its peculiar properties or becomes inactive when heated one-half hour at 60° C. Altogether such a leucotoxic serum induces upon injection a leucopenia lasting from one to one and one-half hours, very similar to that caused by injections of foreign sera or albumins. Following the leucopenia there is a reaction with hypoleucocytosis lasting for four or five hours.

GENERAL BACTERIOLOGY.

Bacteriology of the Nose. In an extended investigation of the bacteriology of the nose Hasslauer[1] reaches the following conclusions: Most of the bacteria drawn in with the breath are arrested in the anterior nares, while the posterior nares shows only a limited bacterial flora. Saprophytes are numerous in the anterior nares. Primary, acute and secondary rhinitis occurs in the acute infectious diseases as a catarrhal inflammation quite analogous to middle-ear and pharyngeal extensions.

No specific organism was determined as the cause of rhinitis. The rhinitis that developed during the course of a specific infection and was caused by a specific bacterium gave only the symptoms of an ordinary cold.

The finding of the meningococcus on the nasal mucous membrane was only possible in a portion of the cases of epidemic meningitis. This organism does not cause a rhinitis. The presence of the meningococcus was demonstrated in the nose only in cases of meningitis or in those who were in contact with such cases and not in other persons. Transmission takes place as a mouth to mouth infection. The mouth and the nose are the atria for this disease. As to the manner of internal dissemination nothing definite was learned, but the finding of the organisms

(1) Centr. f. Bakt., Originale, Aug. 7, 1906.

in the blood would indicate that it occurs through the blood. Simple microscopic examination of nasal secretion for meningococci is impossible because of the presence of similar organisms, especially micrococcus catarrhalis. Cultural and agglutination tests are the only means of demonstrating the presence of meningococci.

Bacteriology of a Common Cold. Benham[1] has made bacteriologic examinations of the secretions from the nose in a series of cases of acute coryza. In the nature of things the bacteria of the colds of one season are not of necessity those of another. The same is true of colds in different localities. Furthermore, it will always be difficult to determine the relative importance of the different bacteria found in a given case. Contrary to expectations, not many influenza bacilli were found. They were present only in two cases. Diphtheroid organisms were found in 95 per cent. of the cases. Cocci negative to Gram were found in 48 per cent. and cocci positive to Gram in 67 per cent. Some of these were pneumococci.

The Nature of Bacteria of the Mouth and the Leptothrix Racemosa. Filandro Vincentini,[2] the discoverer of *Leptothrix racemosa,* has given a succinct sketch of this organism in a paper read before the Section on Stomatology of the American Medical Association at the Boston meeting, June, 1906. The most important feature in his work is his demonstration that the bacteria of the mouth are not true and complete "organisms," although endowed with a power of multiplication by fission, but rather "simple scattered particles" of a more complex organism, *Leptothrix racemosa.* The conception that bacteria are simple "monocellular organisms" is still met with in modern treatises on the flora of the mouth, but Vincentini's work is gradually modifying some of our fundamental conceptions concerning the nature of bacteria.

In recent years the morphology of bacteria has received a great deal of attention. At a meeting of the Royal Society of London, Klein showed photographs of tubercle bacilli presenting distinct branches not unlike a mycelial fungus; from this finding he inferred that at least a few

(1) Brit. Med. Jour., May 5, 1906.
(2) Medicine, Vol. XII, No. 8, August, 1906.

schizophytes are really forms of development or "passing phases" of superior organisms. His observations were confirmed in old cultures of tubercle bacilli by Fischel, Coppen-Jones, Bruns, Semmer, Babes, and Levaditi, and, in the case of diphtheria bacilli, by Kanthack and Fraenkel, so that both bacilli are now conjectured by many observers to be nothing but a life phase of some cladothrix or streptothrix species.

Professor Gunther believes that the branching forms represent a degnerate phase of the single bacilli. Williams and others, on the contrary, hold that the rudimental bacilli are due to a degenerate phase of mycelial fungi or of higher bacteriaceæ. It is clear that in either case their life history could not be confined merely to the monocellular and dissevered state, and that their laboratory habits no longer could serve as a basis for their botanical identification.

It is surprising that hundreds have worked on the white deposit of the teeth, the so-called *Patina denturia* (*Matèries alba* of Leeuwenhoek), before this important organism was discovered by Vincentini. It seems that because of the methods in vogue in bacteriological technique the fruitful heads of racemosa were systematically, though unintentionally, destroyed by an excessive trituration of the specimens upon the slide, so that the various particles were dissociated and gave the appearance of so many independent beings. Besides, the method of mounting all bacteriologic specimens in balsam is almost certain to destroy the fructification heads of the *Leptothrix racemosa.*

As described by the discoverer of the organism, the *Patina denturia* is composed of two distinct layers. The upper layer embraces the tufts or aerial-like appurtenances of the growth, and the lower layer is the portion in close contact with the tooth. Under the name *Leptothrix buccalis* these layers have been previously described by Robin, who saw in them merely an assemblage of barren filaments and granules, and considered the whole growth a filamentous alga.

The upper layer of this growth is composed of a number of fruitful heads. These resemble very minute pedicillar fungi, and the writer found that their number on the

whole human denture approaches nearly a trillion and six hundred billions. Each element of the racemosa fruitful heads embraces five appurtenances, as follows: 1. A central, slender, pale stem, containing internal parietal gemules, invisible in iodin solution but very distinctly observable under gentian-violet; to the central stem, belong, in order of development. 2. The sterigmata or pedicles destined to bear. 3. The sporules. The pedicles are invisible under common object-glasses, being very slender and pale. The sporules are of globular form, pale in iodin solution, more or less colored in anilin, and usually appear in six longitudinal rows. 4. A viscid substance or glair, in all probability an oozing or secretion either of the spores themselves or of the stem, covers the fruitful heads. 5. Lastly, there are a number of branching threads forming a kind of radicular system.

Alongside the fruitful heads and thriving upon the same felting or matrix, as upon a common soil, there are two other forms of aerial-like threads, and these are (a) the younger filaments, or paraphyses, and (b) the male organs.

The deep layer of the racimosa growth is described by the writer as composed of two distinct elements: 1. The "lower stumps," growing as *Bacillus buccalis maximus* of Miller, and, 2, the matrix itself. At its turn, the matrix is seen to be composed of two elements, namely, (a) the chains and bundles representing the *Leptothrix buccalis Maxima* of Miller, and (b) the crowded masses of cocci.

From this short descriptive sketch it will be seen that Leptothrix racemosa is composed of many and complex elements; nevertheless it forms a single growth or entity. The writer concludes that most of the scattered bacterial elements of the mouth are of common descent.

Bacteria in the Mouth. Rucker[1] reports that he has found streptococci and diplococci in the throat of healthy persons. *Streptococcus mucosus* was found in 70 per cent. of all cases examined. Pneumococci of atypical varieties occurred in 50 per cent. of the twenty examinations made while typical pneumococci were found five times, or 25 per cent., in this series.

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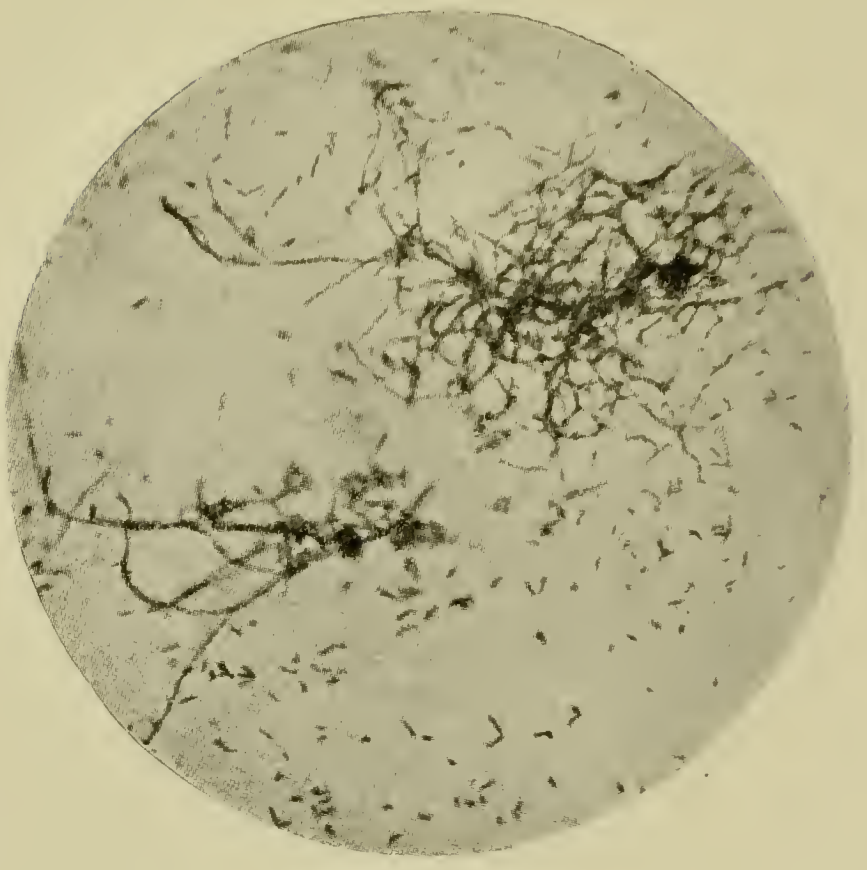
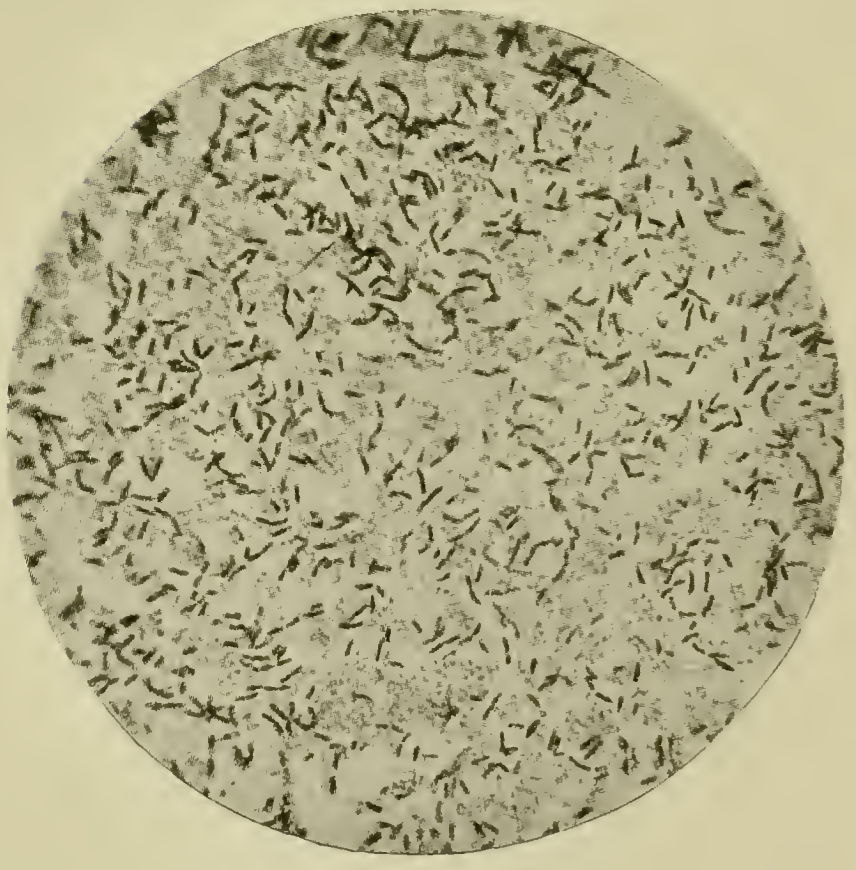
(1) Univ. of Penn. Med. Bull., October, 1906.



Bouillon Culture, 6 Days Old.



Agar Culture, 6 Days Old.

PLATE V.

Bacteria in Intestines. Rindone[1] concludes that bacteria pass through the intestinal wall only when it is necrotic. Injuries of various kinds are not as liable to allow the passage of bacteria as necrosis due to strangulation. Either the serous or muscular coat may be destroyed and yet bacteria do not find opportunity to pass. Any serious lesion of the mucous coat allows bacteria to pass readily to the mesenteric glands or the circulating blood.

SPECIAL BACTERIOLOGY.

Atypical Actinomycosis. In the multiple abscesses found post-mortem in a case described by Levy[2] a streptothrix organism was discovered, the pus containing small yellowish granules resembling the findings in actinomycosis. Microscopic examination failed to show the typical ray arrangement, as the organisms were arranged in tangled masses and showed marked irregular staining. Great pleomorphism was revealed by cultures of the organism, while the Gram and other stains were taken only with the greatest irregularity. The cultures were found to be pathogenic for guinea-pigs and rabbits, and inoculation caused a moderate blood infection. Plate V shows the cultures.

Bacillus flavo-aurantiacus Sporagenes. A new species of bacterium is described by Klimenko.[3] During the examination of samples of antisyphilitic serum (de Lisle) it was found as a contamination. The chief microscopic and cultural characters are as follows: Long, slender bacilli with rounded ends, motile and sporulating. It is stained readily by all anilin stains and is gram positive. On stained slides the bacilli are seen arranged singly and only occasionally in twos. It is aerobic and has a temperature optimum at 37° C. Colonies on agar resemble proteins. The surface colonies are irregular and have a yellow or brownish color. On gelatin as soon as the colonies appear there is liquefaction and the irregularity of the margins of the colonies disappears as the colony grows.

On potato the growth is shining yellow or brownish.

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(1) Rif. Med., Vol. XXI, No. 18.
(2) Deutsche med. Woch., Nov. 1, 1906.
(3) Centr. f. Bakt., Erste Abt. Orig., Sept. 18, 1906.

Milk is coagulated into a firm coagulum with much serum, a film is formed on the surface and an acid reaction results.

In Petruschky's whey acid is produced at first and later an alkaline reaction develops.

Egg and serum albumin are decomposed.

In sugar media acids are formed.

Inol is not produced.

Hydrogen sulphid is formed.

It is not pathogenic for animals.

[It would appear from the description that this organism belongs to the potato bacillus group. This is also another example of the improper and unscientific naming of bacteria that is in vogue.—Ed.]

Spirillum Choleræ. In the course of bacteriologic examinations of cadavers of pilgrims in the east Prochnik[1] found that cholera vibrios were present in 6 of the 38 cadavers examined. These cases had all had dysentery but there was no evidence of a cholera epidemic. The cultures from the intestines showed that the bacilli were virulent.

The Dysentery Bacillus in Infantile Diarrhea. J. H. Mason Knox and E. H. Schorer[2] found some form of dysentery bacillus present in 70 per cent. of cases examined. The general conclusion drawn from their observations was that the etiologic factors were not responsible for clinical or even for pathologic types.

Antidysenteric Serum. There are two important clinical forms of dysentery having distinct etiologic factors and causing definite, characteristic lesions. One is caused by the *Amœba dysenteriæ* and is a form of dysentery peculiar to tropical lands, causing abscess of liver; and the other is of microbian origin and is caused by a specific organism. The latter form of dysentery is frequently met in the countries of the temperate zone, and never causes liver abscess. It occurs in epidemics, is easily transmissible, and at times very contagious. Frequently it causes a very high mortality. In Japan, according to Shiga, the average mortality caused by it between 1878

(1) Wien. klin. Woch., Vol. XVIII, No. 39.
(2) J. E. M., May, 1906.

and 1900 was 24.2 per cent. In Moscow mortality oscillates between 12 and 17 per cent. for adults only. It is as frequent, and at times more frequent, in some parts of Germany, and during the winter of 1899 its mortality in England varied from 20 to 50 per cent.

For these reasons some very serious efforts have been made to find out a specific form of treatment. Shiga, in 1898, was the first to make investigations with this end in view. Kruse, having isolated the bacillus of dysentery in Germany, attempted the same work. Both investigators immunized their animals by subcutaneous inoculations of cultures. Their serum showed some antibacterial properties, but remained inefficacious because the disease gives rise also to an intoxication, which remained uninfluenced. L. Vaillard and Ch. Dopter[1] mention the results obtained in the treatment of dysentery with the serum of Rosenthal, who, at last, succeeded in obtaining the desired endotoxin element by means of maceration and autolysis of the bacilli. One hundred fifty seven patients were treated at a hospital in Moscow; of these, only 7, or 4.5 per cent., died, while at the other hospitals of Moscow the mortality was 10 to 11 per cent., and, according to the official statistics for Moscow, the average mortality due to dysentery for the preceding ten years varied from 12.2 to 17.5 per cent. for adults.

The serum was also used in the Russo-Japanese war with results equally satisfactory.

Vaillard and Dopter report on a horse serum prepared by them which they consider superior because it possesses preventive as well as curative properties and is equally efficacious against the bacillus of dysentery and its toxin. This is easily proven by experiments on rabbits. The subcutaneous inoculation of a rabbit with the culture causes its death in 3, 4 or 5 days, and the pathologic changes in the system are a true reproduction of the lesions caused by dysentery in man; the injection of toxin obtained by proper filtration will either cause death in a few hours or only illness lasting several days, according to the dose used. The rabbit is therefore well suited for such experiments.

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(1) Annales de l'Inst. Pasteur, Vol. XX, No. 5, May, 1906.

The writers found that a dose of ½ c.c. of serum administered 24 hours after experimental infection with a quantity of virus known to cause death in four days (4 c.c. of a 24-hour-old bouillon culture) invariably insured recovery; all control rabbits died on the third or fourth day. The treated rabbits preserved their normal state after a slight temporary illness. Experiments intended to show the preventive effects of the serum gave similar uniform results. When the toxins are used for inoculation the results are the same, but the serum must be given in larger doses.

A mixture of equal parts of toxin and serum remains ineffective whether it is injected subcutaneously or directly into the general circulation.

The combined antibacterial and antitoxic properties of the horse serum were also proven clinically on man. Ninety-six adult patients were treated with this serum exclusively, and only one died.

Light cases, such as would recover easily by ordinary therapeutic measures, were not placed under this specific treatment. The patients were classified, not according to the fever—as dysentery is not a characteristically febrile disease—but according to the number of bowel evacuations, as follows:

Light cases; 15 to 20 bowel movements per day..... 50
Severe cases; 30 to 80 bowel movements per day..... 18
Very severe cases; 80 to 150 bowel movements per day. 24
Extremely severe case; 150 to 288 bowel movements per day; this is the case that ended in death.

The remedial power of the serum is noted by a rapid amelioration of all the local and general symptoms of dysentery as soon as administered. In a few hours the patient experiences a sensation of well-being. The abdominal pains and tenesmus, except in the most severe cases, disappear within the first 24 hours. The intestinal troubles cease, the evacuations lose their bloody character. Tracings are given of the number of evacuations, and from the first serum inoculation the line takes an almost perpendicular direction downwards. The general symptoms are relieved with equal promptness. Recovery is estab-

lished in 2 to 3 days for the average cases, and in 4 to 6 days for the most severe cases. Of four patients who were in a dying condition before taking the specific treatment, three recovered, in 8, 11 and 20 days respectively; the fourth died on the thirteenth day.

Gonococcus. Thayer[1] cultivated the gonococcus from a case of endocarditis during life. In a second case the cultures were negative. In both pure cultures of gonococcus were obtained from the heart valves postmortem. The first of these cases is to be considered as an instance of gonorrheal septicemia.

Serum Therapy. Torrey[2] reports the use of an antigonococcus serum in the treatment of gonorrheal rheumatism. This class of curative sera has not proven of much interest because there is no evidence of immunity to gonorrhea, infection of lower animals is very doubtful and the cultivation of the organism is most unsatisfactory. Again it is certain that the toxins of this organism are endotoxins necessitating that the cells inclosing the cocci die and dissolve to bring about a free toxin. The antigonococcus serum was prepared by the writer by first growing the gonococcus derived from an acute case on a mixture of ascitic fluid and slightly acid beef infusion peptone broth. The cultures were incubated at 36°—37° C. Large rabbits were used for producing the serum. They were inoculated at intervals of four days with 10 c.c. of the cultures given intraperitoneally. Young cultures as well as old ones gave the same results. After six inoculations had been given the animals were bled, usually from the ear veins, and about 60 c.c. of serum obtained after the blood coagulated. The protective action of the serum is evidenced by the following experiment: Two pigs were given 1 c.c. of serum and one pig 2 c.c. respectively. Eighteen hours later these three pigs were each given 3 c.c. of toxins and in addition a control pig was given a like amount. In one hour the control pig showed a fall of 10 degrees in temperature and died in three hours.

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(1) Am. Jour. Med. Sc., November, 1905.
(2) Jour. Am. Med. Assoc., Jan. 27, 1906.

Rogers reports (in the same place) the results of treating patients with this serum.

Bacillus Chlorhydrici. Palier[1] describes a bacillus isolated from the stomach which he has named *Bacillus chlorhydrici.* This organism is normally present in the stomach and usually aids digestion, but it may become pathogenic, and, the writer thinks, it may be a cause for ulcer.

The organism is a slender, small bacillus, slightly motile and negative to Gram's staining method. Spores are absent. It is especially abundant in hyperchlorhydria.

Bacillus Pestis. *Antiplague inoculations, vaccination.* Kolle and Strong[2] describe the use of an attenuated culture of living bacilli. The best means of attenuation were found by these writers to be cultivation at a temperature of 41° to 43° C. and by the introduction of from 0.5 to 5 per cent. of alcohol. The attenuation was carried to such a degree that one million times the usual lethal dose could be injected into guinea-pigs without causing death or even illness. In the animals such injections developed a high degree of immunity. Small doses, one one-hundredth of a loopful, were first injected into persons by Strong in Manila. In all 42 persons were vaccinated. No deleterious effects beyond a slight local swelling and some rise in temperature were observed. The presence of immunity in the vaccinated persons was shown by the presence of specific agglutinins in their sera for virulent plague bacilli and the transfer of immunity to experiment animals. This vaccination method was tested on monkeys by subsequent injections with virulent bacilli and it was found that bacilli were present in the tissues for six to eight hours after inoculation, but after 24 hours all cultures made from the tissues remained sterile.

The advisory committee (India) concludes as regards the transmission of bubonic plague that fleas are of first importance. Experiments with guinea-pigs showed that when these animals were allowed to run free in plague houses they attracted a large number of fleas, which were mostly rat fleas. Some of these animals contracted plague

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(1) Amer. Med., Feb. 24, 1906.
(2) Deutsche med. Woch., March 15, 1906.

and died. When guinea-pigs were let loose in a plague house after disinfection they still collected numbers of fleas and some became infected and died. Fleas that were taken from plague infected rats found dead in such houses were able to transmit plague to healthy animals. Fleas collected by guinea-pigs in plague houses could be taken from their hosts and transferred to fresh fleas and thus induce new infections. Animals placed in plague houses in pairs, one protected by screening and the other not, showed that no protected animal developed plague while several of the unprotected animals died of plague. Other pairs of animals placed in plague houses, one protected by a layer of fly-paper, the other not, showed that fleas were caught on the fly-paper and the guinea-pigs escaped infection. Some of the other pigs died of plague. The examination of fleas for plague bacilli showed one infected out of 85 human fleas and 23 infected fleas out of 77 rat fleas examined.

Bacillus Equi. This bacillus is described by Klein.[1] The animal—a private carriage horse—had been in the owner's possession for two and a half years and had not been laid up ill during that period. The horse was at work in the afternoon, returning to the stable at 5 p. m., and died at 7:45 the same evening.

The following were the chief symptoms at the post-mortem examination: There was blood about both nostrils and the abdomen was swollen; the mesentery was inflamed in patches, with blood extravasations; there were inflammatory patches along the large bowels, the vessels were congested with extravasations, the mesenteric blood vessels were engorged, and the lungs were congested. Film specimens of the blood showed a great many small and large groups of bacilli; in these groups there were some not larger than a coccus, others long cylindrical, and all intermediary forms. From this it was therefore evident that preliminary diagnosis, "not anthrax," was correct. Klein injected subcutaneously in the groin of a guinea-pig (1) a fair dose of the blood—about 0.1 c.c. This guinea-pig developed a soft swelling in the

(1) Jour. of Hygiene, September, 1906.

groin and on the abdomen of the injected side, but on the fourth day seemed quite lively. The animal was killed and on post-mortem examination showed about the seat of injection gelatinous infiltrations from which a large amount of turbid sanguineous fluid oozed out. Under the microscope the fluid, besides containing blood corpuscles, was crowded with short bacilli, some free, others in groups, some almost spherical, like cocci, others longer or shorter cylindrical; they were non-motile; gram negative. Cultures: surface agar plate, agar tube, and gelatin tube proved that the fluid contained one species only of microbes, non-motile, gram negative, from 0.8 to several micromillimeters in length, in shape of all forms intermediate between coccus-like and cylindrical up to several μ. It was therefore quite clear that this result negatived anthrax. All the viscera of the above guinea-pig appeared to be normal. With a single colony from the above agar plate injected subcutaneously in the groin one further guinea-pig (2). Next day this animal showed a soft slight swelling about the seat of injection. After another day the swelling had slightly increased, but the animal seemed quiet and off food. Four days after the injection it was in a dying condition. The post-mortem examination showed the following appearances: locally there was slight edema and congestion; the spleen was enlarged and dark; on the parietal pericardium and the mediastinal pleura there were purulent pseudo-membranes; the lungs were much congested. Films and specimens of the pseudo-membranes showed, besides the leucocytes constituting the pseudo-membrane, crowds of the bacilli, many intracellular, others free. In shape, size and staining they were of the same characters as those used for the injections. Cultures made of a trace of the pseudo-membrane yielded pure cultures of the same species. Film specimens and cultures of the spleen showed great abundance of the same microbes. The heart's blood contained the microbe also in large numbers, platinum loop of the blood yielding an almost confluent mass of colonies. With a single colony from an agar plate of the heart's blood of this guinea-pig he injected subcutaneously one large rabbit. The animal died four days after; it had local inflammation, thin pseudo-membranes on the liver and an enlarged

spleen, pseudo-membranes on the mediastinal pleura and the pseudo-membranes of the liver, the spleen, and the pleura showed in film specimens and culture abundance of the bacilli; a similar result was obtained with tissue of the spleen; the heart's blood also contained great abundance of the bacilli.

From these experiments it follows that the original blood of the horse contained in abundance a microbe which proved pathogenic and fatal to the guinea-pig and through this to the rabbit, the microbe in small doses (a single colony) causing death in four days with pseudo-membranes on the viscera, with abundance of the same microbe in the pseudo-membranes, the heart's blood, and the spleen. The microbe, for which Klein proposes the term *"Bacillus equi,"* resembles in shape and size the *Bacillus pseudo-tuberculosis* (A. Pfeiffer), possessing all intermediate shapes between a coccus and a cylindrical, almost filamentous bacillus and being non-motile and not liquefying gelatin, but in action it obviously differs from it, the former causing acute illness and not producing the well-known necrotic nodules in the spleen, the liver, and lung, and the lymph glands characterizing the action of the *Bacillus pseudo-tuberculosis.* The *Bacillus equi* grows well at 37° C. and at from 20° to 21° C. it forms round, more or less flat, moist, translucent colonies both on agar and on gelatin; it grows slower and is distinctly more translucent than *Bacillus pseudo-tuberculosis.* The *Bacillus equi* is practically gram negative; the oval forms, both of culture and of the animal tissues, show bipolar staining with methylen blue. The *Bacillus equi* does not alter neutral red broth, litmus milk, lactose peptone, or litmus glucose bile salts (MacConkey fluid). In alkaline beef broth it forms slight but uniform turbidity; no pellicle. *Bacillus pseudo-tuberculosis* leaves the fluid fairly clear but forms copiously granules and flocculi with a pellicle on the surface (where the fluid touches the glass). The *Bacillus equi* does not form spores and is devitalized by complete drying. Gordon subjected in comparative series both the *Bacillus equi* and the *Bacillus pseudo-tuberculosis* to the various sugar tests and he found as the chief and constant differences that while *Bacillus pseudo-tuberculosis* forms acid from maltose and not from saccharose the *Bacillus equi* behaves

in a contrary way, inasmuch as it forms acid from saccharose but not from maltose.

As already mentioned, the action of the *Bacillus pseudo-tuberculosis* and of the *Bacillus equi* is fundamentally different. As a further distinction may be mentioned the fact that while *Bacillus pseudo-tuberculosis* retains its pathogenic action unimpaired in subcultures after many months' transference the *Bacillus equi* rapidly loses its virulence in subcultures. The microbe of fowl cholera, with which the *Bacillus equi* has certain morphologic and cultural characters (including indol formation in broth) in common, differs from this microbe in (a) the bacillus of fowl cholera is virulent for mice and non-virulent for guinea-pigs, the *Bacillus equi* is virulent for the guinea-pig and non-pathogenic for mice; and (b) the bacillus of fowl cholera curdles milk and reduces litmus and the *bacillus equi* does neither; milk remains fluid and litmus remains unchanged.

B. Diphtheriæ. *General paralysis.* Eyre[1] examined patients in asylums with a view of learning the possible relation of diphtheroid organisms to general paresis. He could not establish any relation. He found the incidence of the diphtheria organisms in the throats of insane to be 17.3 per cent., or not far different from the sane (18.5 per cent.) population. The genuine *B. diphtheriæ* was found to be 5.07 per cent. in the insane, which is again somewhat lower than that for the healthy sane (6.9 per cent.). Among general paretics the result was 5.0 per cent. for presence of *B. diphtheriæ* and 5.1 per cent. in other forms of insanity.

Diphtheria Toxin in the Blood. Uppenheimer[2] was able to show the presence of diphtheria toxin in the blood of six out of fourteen patients examined. Four were doubtful and four were negative. The finding of toxin in the blood shows the need of additional antitoxin. When the amount of antitoxin given is large it can extract toxin from the tissues and render it inert. The infiltration of the subcutaneous tissues at the point of injection was taken as evidence of toxin action.

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(1) Brit. Med. Jour., Oct. 28, 1905.
(2) Muench. med. Woch., No. 33, 1906.

Antidiphtheria Serum. It is proposed by Bandi[1] that an improved diphtheria serum that should have antibacterial as well as antitoxic properties would be of value. His serum designed with this end in view he calls bivalent. It is antitoxic and also contains bodies which the writer likens to the opsonins of Wright. Under its influence the bacteria are prepared for phagocytosis. No special bacteriolytic action of the serum towards the bacteria is claimed. It is stated that this serum has been put up in pastilles for administration by mouth. Disappearance of the membrane and bacilli from the throat results when the pastilles are allowed to dissolve slowly in the mouth. A mixture of the serum and antiseptics is also rubbed over the infected areas. In some cases also infection of the nose was treated by dropping the serum into the nostrils. It is also advised that in laryngeal diphtheria instillations into the larynx and trachea be made. Cases are recited and reports of others regarding the value of this serum are presented.

Fusiform Bacilli. Lewkowicz[2] further describes his results in cultivating fusiform bacilli. The writer claims priority over Ellermann in regard to methods of cultivation. However, he modifies all earlier methods by using glucose agar instead of his horse serum. Growths are only obtained under anaerobic cultivation. In the glucose agar serum mixture colonies develop in the deeper layers but not on the surface. The presence of blood serum is absolutely essential for growth. If three tubes are inoculated, the first two of glucose agar and a third containing serum, a few colonies may appear in the first because of transference of some serum from the source of inoculation; the second, however, is negative, but the third will show excellent growths, as may be seen in Plate VI.

Considerable variation is seen in microscopic study of the bacilli and only in young cultures is there any decided regularity. Their length is widely different and sometimes they are in pairs. They stain poorly and with much irregularity. With Gram method the result is negative. Single colonies which appear in the medium reach a size of $\frac{1}{2}$ mm. and develop parietal outgrowths. These out-

(1) Il Policlin., July, 1906.
(2) Centr. f. Bakt., Orig., May 17, 1906.

growths are more marked on colonies nearer the surface of the medium and the outgrowths themselves tend towards the surface.

Bacillus of Leprosy. Emile Weil[1] reports that he has had positive results in the artificial cultivation of *B. leprœ.* However, the cultures showed growth only upon the first inoculation and it was impossible to continue it in subcultures. Development was evident in about 5 days and continued for 15 to 20 days, after which the culture died. The medium used consisted of broth, 1 liter; glycerin, 40 grams; glucose, 8 grams; peptone, 10 grams; agar, 20 grams. One part of egg yolk and four parts of the above were mixed and carefully sterilized at about 80°—85° C.

Meningococcus. The origin and nature of the infection in cerebro-spinal meningitis is discussed by Vansteenberghe and Grysez.[2] A comparative study is presented between the meningococcus isolated from a case of epidemic meningitis and certain cocci found in the nose. Inoculation experiments made with cocci isolated from the nose resulted in meningitis analogous to infections caused by subdural inoculations with the meningococcus. This infection is to be considered as an auto-infection with cocci present in the nose much after the manner of pneumonia caused by cocci in the sputum which ordinarily have no effect. In studying the action of Gram staining method it was found that much depended upon the condition of vitality of the cultures. Unfavorable conditions interfere with the staining by this method. This procedure, therefore, cannot be held as having much diagnostic importance. The point has more bearing upon the examination of cultures than upon the examination of specimens obtained directly, by means of spinal puncture.

Baldwin and Goodwin[3] state that the meningococcus is present in the nasal mucus in 50 per cent. of cases during the first week. Later in the course of the disease they disappear. This coccus is also present in about 10 per cent. of those in contact with cases. The transmission takes place through the mucus of the nose being dissemi-

(1) Ann. de l'Inst. Pasteur, December, 1905.
(2) Ann. de l'Inst. Pasteur, January, 1906.
(3) Medical News, Dec. 30, 1905.

nated, but some factors in the individual are apparently necessary to induce an infection. The writers can see no connection between cerebro-spinal meningitis in other animals and the epidemic form in man. It is not carried by vermin or insects, nor does it appear to be a house infection.

Ohlmacher[1] prepared the poison of meningococci by first cultivating the organism upon a glucose chalk bouillon medium. Glucose in 0.5 per cent. amounts and chalk in 1 per cent. amounts were added to ordinary beef bouillon. Cultures were made in Fernbach flasks in order to provide for large surface growth. The growth takes place luxuriantly upon the surface and by neutralizing the acid with the chalk the vitality of the bacteria is preserved for three to six weeks. Trikresol is now added and the mixture filtered through paper.

The subcutaneous injection of these toxins caused local swelling and sometimes abscesses. To avoid the formation of abscess the infection was made intravenously. A horse that was injected with living meningococci cultures showed profound intoxication and died in 18 hours. Meningococci could not be recovered from the blood. Three horses were now injected; one with living culture one-half 6 days, and the other half, 13 days old. This animal died in 14 hours. The second horse received one-half, 10-day dead culture and the other half, 6-day living culture. This animal lived 62 hours. The third received the toxins above described. The toxic effect was similar to that in the other cases, but the animal recovered. The filtering of the trikresol culture through porcelain filters removes the toxic properties from the filtrate.

The symptoms resulting in injected animals are essentially of a nervous character. Shortly after the injections the horse shows weakness of the hind legs and stands insecurely, gradually increasing muscular tremors appear and finally distinct clonic convulsions of large groups of muscles. When the animal falls it never rises again. The animal shows great sensitiveness to noise and touch. Death is due to exhaustion.

Cerebro-spinal Meningitis. The epidemic of cerebro-

(1) Jour. Am. Med. Assoc., July 21, 1906.

spinal miningitis in New York in 1904-5, during which some 4,000 cases were observed, leads Flexner[1] to the investigations recorded. The *Diplococcus intracellularis* possesses characters that make its identification certain. The points of distinction from other Gram negative cocci are in the appearance of the growths on media, the action on sugars, and the brief vitality of the cultures. Five or six days is the average period for survival of any considerable number of cocci in a culture. Irregular staining is also a marked feature in cocci from older growths. Dissolution or autolysis of the bacteria takes place with rapidity when the culture dies. When the cocci are heated to 65° C. this change is suspended, indicating that it is a ferment action. This peculiarity of the organism is an important means of distinguishing it from other similar organisms, especially *Micrococcus catarrhalis.* A considerable number of cultures of Gram negative cocci were compared by the writer with his cultures, and it was found that they did not have this autolytic activity, and also that they grew upon media not having blood serum in them, and retained vitality for considerable periods.

The cultures that have undergone autolysis are toxic, and the fluid portion obtained either by filtration or centrifugation will kill young guinea-pigs. The pathogenic action shows considerable variation, some stains giving negative results. Freshly isolated cultures are the most pathogenic, but become inert sooner or later. No increased activity was observed after passing cultures through numerous generations.

Active cultures injected into the peritoneal cavity will often cause death in 8 to 10 hours. Post-mortem findings show fluid exudates with more or less fibrin deposited on the liver and omentum and hemorrhages in the mesentery and diaphragm. The pleural cavities contain some clear fluid. Cocci are present in the exudates, from small numbers to very great numbers, but there is an activity of bacteriolysis which tends to increase the toxicity of the exudates. Meningitis with characteristic symptoms was produced in monkeys by intraspinal injection. Inoculation at a low level of the spinal canal was followed by the

(1) Brit. Med. Jour., Oct. 20, 1906.

spreading of the cocci to the meninges at the base of the brain. The condition in the spinal canal of monkeys resembled very closely the changes in the peritoneum of the guinea-pigs, except that a larger number of polynuclear cells were present. Some of the animals survive after being acutely sick for a few days. It may happen that the animals die without showing cocci in the spinal fluids, as also happens in guinea-pigs. This is because of the dissolution of the organisms. Antisera were prepared by injecting various animals, but the goat was found to produce the best serum. Intraspinal injections of these sera arrested the disease in experimentally inoculated animals. A few failures occurred, and it is impossible to offer an adequate explanation for them.

Malaria. *Melaniferous Leucocytes.* Clemens[1] calls attention to the value of pigment granules in leucocytes, as described by Manson, in the diagnosis of malaria. Light yellow or red pigment granules are found in less severe malaria infections, while black granules show the æstivo-autumnal type. The number of granules in the cells also indicates the duration of the infection as it increases until in long standing cases the cells are crowded with pigment. This observation may often give a positive diagnosis when the examination for plasmodia is negative or unsatisfactory.

Morax-Axenfeld Bacillus. Gifford[2] considers this bacillus of more importance than is generally held. Examination of the small masses of mucus in the angle of the lids will often show a number of these bacilli. The chronic form of this infection would be considered as trachoma unless microscopic and cultural examinations establish the true diagnosis.

Bacillus Mallei. Robins[3] describes the isolation of *B. Mallei* from a case of chronic glanders. The points of interest in the cases observed are mainly in the very chronic character of the infection and the atypical lesions. The development of rash in the case was very slow and treatment very unsatisfactory. There was also a peculiar

(1) St. Louis Med. Review, June 30, 1906.
(2) Ophthalm. Rec., November, 1905.
(3) Studies from Royal Victoria Hospital, Montreal, Vol. 2, No. 1, May, 1906.

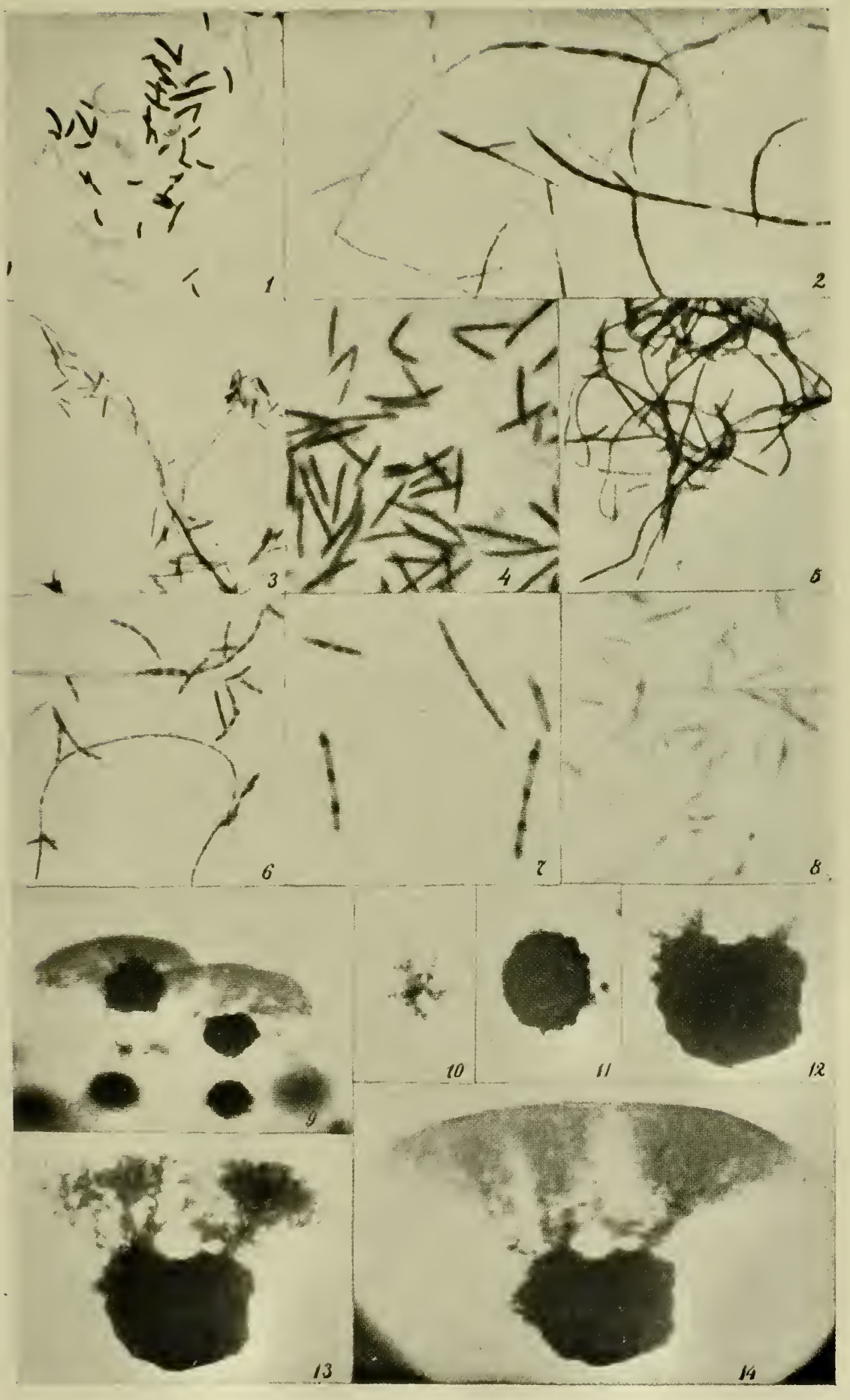
white urticaria-like edema around the lesions. The deeper lesions resembled gumma. The process here was essentially the breaking down and liquefaction of tissue, while secondarily a moderate amount of suppuration occurred. After long periods of slow improvement of the lesions a rapid necrosis of tissue was likely to occur. In 48 hours the repair of six weeks would be destroyed. Antiseptics were of no value. The lesions generally contained pure cultures of the glanders bacillus and after being opened did not tend to harbor secondary infection. The disease was very chronic and was under observation at least 20 months. The extension was by way of the lymphatics and also by the blood; however, the latter was the more important route. The case presented a very low degree of contagion. Possibly two other persons were infected. In this case there were no nasal or pulmonary symptoms in contrast to the localization in the horses. The inoculation of male guinea-pigs resulted in typical infections, including the usual orchitis.

Rabies. *Action of Radium.* Tizzoni and Bongiovani[1] applied the rays of radium to the serum of rabies and to the eyes of rabbits into which the virus had been injected. It was found that radium exerted a rapidly destructive action upon the virus. One hour's exposure caused attenuation and after a longer exposure it became inert. In the animal experiments it was found that when exposures to radium were made simultaneously with the introduction of virus or within one or two hours, cure might be expected, but if a longer period, such as twenty-four hours, intervened, the treatment was without effect.

Negri Bodies. Materazzi[2] says that the finding of Negri bodies in the fresh hippocampus is sufficient for a diagnosis of rabies. The diagnosis can be made in 24 hours. He considers that the etiologic relation of these bodies has been established.

The importance of the discovery of Negri bodies in the cells of the central nervous system in hydrophobia is discussed by Bongiovanni.[3] The finding of these bodies has made rapid diagnosis a possibility and has removed much

(1) Rif. Med., May 6, 1905.
(2) Gaz. degli Ospedali, No. 36, 1906.
(3) Centr. f. Bakt., Originale, June 2, 1906.



Bacillus Fusiformis.

PLATE VI.

of the uncertainty regarding rabies that formerly existed. The nature of these bodies is still in doubt. They have been considered as the causal agent in the disease and also as the simple result of cellular changes. The writer's observations are confined to the determination of the changes in and presence of Negri bodies in the central nervous system of animals inoculated with a fixed virus. Portions of the hippocampus major, cerebellum and Gasserian ganglion were taken for microscopic sections. These were hardened 24 hours in Zenkers' fluid, washed 12 hours in water, hardened in alcohol, penetrated by xylol and xylol paraffin and imbedded for sectioning. The staining method employed was that of Fasoli, the steps of which are as follows:

Watery eosin solution 5—10 minutes.
Wash thoroughly in water.
Differentiation by alcoholic solution of sodium hydrate (4—5 drops of caustic soda in 50 per cent. alcohol.)
Wash in water.
Stain in water-methylene blue solution.
Alcohol dehydration, xylol and balsam mounting.

The results of the observations showed that where the fixed virus was used and the rabbits died in 6—8 days, or in a few instances as late as 20 days, no Negri bodies were found. Sections from the rabbits inoculated from dogs or those dying in 20—30 days always showed Negri bodies. The findings are so characteristic that it is possible by this means to state whether a fixed virus or the ordinary street virus of rabies had been used on the animals.

The rapidity of the infection cannot account for the difference. Either the bodies are entirely absent in the infectious and fixed virus or there is a different development of the parasite in the two infections not demonstrable by present methods.

Streptococcus Mucosus. The differentiation of streptococci has generally been a matter of difficulty; recently, however, by the aid of the Schottmüller blood agar method it has been made possible to distinguish several species. The *Streptococcus mucosus* described by Schott-

müller has been investigated by Otten[1] with the aim of ascertaining its pathogenesis. Schottmüller reported six cases of croupous pneumonia in which this bacterium was to be considered as the causal factor. The present article adds seven new cases. Case I, suppurative bronchitis with hypostatic congestion of the lower lobes; II and III, cases of bronchopneumonia; IV, croupous pneumonia; V and VI, suppurative meningitis, and VII, suppurative pelvo-peritonitis complicating syphilis of the rectum. In five of these cases the streptococcus was isolated from the blood in addition to the findings from local material. All microscopic, cultural and pathogenic characteristics corresponded entirely with the findings as featured for this organism.

Tangemeister[2] experimented with antistreptococcus serum as a prophylactic measure in various conditions: operations, labors, etc. He believes that the serum acts specifically but that it is not antitoxic. Injections of serum cause increased phagocytosis. Under a number of circumstances, however, the immune bodies are destroyed, when the number of streptococci is large, when they are so located as to be protected from the leucocytes and when the streptococci are very virulent. From his observations the writer concludes that nothing of a beneficial nature can be attributed to such infections as regards immunization. Further than this he doubts their curative value.

Parameba. Craig describes a parasite found in the intestinal contents of six native patients in the Philippines. Watery stools containing some blood and mucus were the chief clinical findings. The name *Parameba bilhardia* is proposed by the writer for this parasite. An ameboid stage of development followed by a flagellate stage was observed in its life cycle.

Spirochæte. *Spirochæte dentium—Pathogenic action.* In view of the interest in spirochæte that is now so general Miller[3] describes a case in which the infection of a tooth pulp could be attributed to *Spirochæte dentium.* Upon splitting a carious tooth and dissecting the pulp Miller found an abscess of pin-head size upon its surface.

(1) Deutsche Arch. f. klin. Med., March 12, 1906.
(2) Deutsche med. Woch., July 5, 1906.
(3) Deutsche med. Wochens., March 1, 1906.

Smears made from the pus and stained with fuchsin show large numbers of spiral organisms and very few cocci or bacilli. Because it was present in such large numbers the writer considers this organism the causal factor. He further offers the proposition that they may find entrance to deeper structures in such infections. Plate VII shows the cultures obtained.

Flagilla on Chicken and Recurrent Spirochæte. Zettnow,[1] following an observation of Borrel in which he demonstrated flagella on chicken spirochæte, presents photomicrographs of *Spirochæte recurrens* from Africa. These, as can be seen, show the flagilla in abundance. His method of preparing the specimens is as follows: The material used is centrifuged and the sediment washed to remove all albumin. Slides are spread and treated with solution of tartar emetic and then with silver ethylamine. A magnification of 1,000 diameters is ample for the demonstration of these structures. See Plate VIII.

Syphilis. *Spirochæte in tissue.* Buschke and Fischer[2] describe the results of staining procedures for *Spirochæte pallida* in the tissues of six cases. These were obtained from children with undoubted hereditary syphilis, all having died during their first half year of life. In one of these cases the organisms were found in numbers in the spleen, liver and kidneys. The staining method employed was that of Bertarelli and Volpino. Following formalin and alcohol hardening, small pieces of tissue were soaked in silver nitrate solution, 1.5 per cent. for three days at a temperature of 38° C. Next, for 24 hours they were brought into:

Pyrogallic acid.....	2 grams
Formol	5 c.c.
Water 100	c.c.

to reduce the silver salt. Paraffin imbedding and sectioning followed. The sections were counterstained with Giemsa stain or toluidin blue. The writers call attention to the presence of numbers of spirochæte without marked histologic changes in the organs. This was specially true

(1) Deutsche med. Wochens., March 8, 1906.
(2) Berl. klin. Wochens., Jan. 1, 1906.

of the bile duct, where the organisms were found both between and within the cells.

Bandi and Simonelli[1] examined five cases of secondary syphilis and found the *Shaudinn spirochæte* in three. Scrapings from papules were used and in one case the findings were positive in blood taken from a cutaneous lesion. The Gram method of staining was used.

Spirochæte in Hereditary Syphilis. Wersilowa[2] had opportunity to examine syphilitic twins and made microscopic sections of the organs and placenta. One of the twins was born alive but died shortly afterwards, and the other was badly macerated.

The findings are shown in Plate IX. There was no evidence of active syphilis in the mother, but sections of the placenta showed the organisms in large numbers. The spirochæte were demonstrated by smears as well as in sections. The specimens were stained by the silver nitrate and the azur-eosin methods.

Metchnikoff and Roux[3] found that it was possible to abort infection with syphilitic virus by making mercurial inunctions within a certain time. The efficiency of this preventive measure was demonstrated on thirteen apes, none of which developed syphilis. Later an experiment was made upon a healthy student. The virus from hard chancres of two patients was rubbed into a scarification of the preputial fold. One hour later an ointment of calomel in lanolin was thoroughly rubbed over the area. Four macaques were inoculated with the same virus. One received a local inunction one hour later, another 24 hours later and the other two no treatment whatsoever.

The student escaped without special lesions, as did also the first ape; the second developed a chancre after a month's time, while the other two showed a typical syphilitic infection.

The writers were also able to prove attenuation of the syphilitic virus by passage through apes. This may lead to vaccination methods. After eight passages through various apes it was impossible to infect a *Macacus rhesus,* but when again inoculated once into a chimpanzee

(1) Gazz. degli Osped., July 16, 1905.
(2) Centr. f. Bakt., Orig., Oct. 29, 1906.
(3) Bull. de l'Acad. de Med., May 8, 1906.

virulence was partly restored and a mild infection developed in the rhesus species used.

Spirochæte Duttoni. The passage of *Spirochæte Duttoni* from the mother to the fetus has been demonstrated by Breine and Kinghorn.[1] The young have no immunity from the mother but promptly become infected when injected with blood containing spirochæte. Ticks were allowed to bite rats and after the usual incubation period of five days the parasites were found in the peripheral circulation.

Staining for Spirochæte. Bertarelli and Volpino[2] recommend the following procedure for *Spirochæte pallida:*

1. Fixation of very small pieces of tissue in alcohol—less than one mm.
2. Soaking for four days in:

Silver nitrate	1.5
Distilled water	50.0 c.c.
Alcohol, 95 per cent	50.0 c.c.
Acetic acid, strong	4-5 drops

Should there be a precipitate the solution must be renewed.

3. Complete washing in distilled water.
4. A 24-hour bath in Van Ermengem's solution:

Tannin	3 grams
Gallic acid	5 grams
Sodium acetate	10 grams
Water	350 c.c.

5. Complete washing in water.
6. Alcohol chloroform paraffin sections. Further staining is not essential.

Nature of Spirochæte Pallida. Saling[3] brings forward some convincing evidence that the structures seen in tissues and considered as the spirochæte of Schaudinn are nerve fibrils. The fact that the silver methods of staining have proven so valuable in the search for the syphilis organism is due to the reaction with nerve fibrils; besides, the reaction is not continuous. Appearances entirely analogous to

(1) Lancet, London, July 28, 1906.
(2) Centralbl. Bakt., Orig., April 12, 1906.
(3) Centr. f. Bakt., Orig., Sept. 1, 1906.

the specimens showing *Spirochæte pallida* are reproduced.

Distribution. Bertarelli[1] describes the findings in syphilitic osteochondritis as regards *Spirochæte pallida.* Descriptions of the sections of periosteum and marrow show the organisms in considerable numbers. The specimens were obtained from cases of syphilis in the fetus. It is stated that in some places the organisms are apparently so crowded by the new bone formation that they are much broken and appear as irregular sized pigments. In other places they have entirely disappeared because of the new bone formation.

Inoculation Experiments. Bertarelli[2] reports the results of inoculation of rabbits with syphilitic material. The inoculations were made in the eyes of the animals and the presence of *Spirochæte pallida* in the tissues was shown. The organisms were present in large numbers, not so much in the center of the infected area but rather at its margin. Considerable leucocyte infiltration was also present. The spirils are in groups, often twisted together and follow the direction of the connective tissue fibrils. In some places the spirals were present at some distance from the area actually involved. The liver impregnation method of staining was used. Illustrations are reproduced on Plate X, showing different stages of infection.

Spirochæte; *Other Forms.* Breinl[3] had opportunity to compare the infections of monkeys with the spirochæte of African tick fever with the *Spirochæte Obermeieri* used by Novy in his experiments. He found that the animals infected with either of these organisms passed through the ordinary course of the infection and had several relapses. Subsequently reinoculations were made and the monkeys were found refractory to the organism that had been used before but not to the opposite one. This would lead to the conclusion that the two organisms are different species. The writer suggests the name *Spirochæte Duttoni* for the organism of African tick fever.

Spirochæte Obermeieri. Novy and Knapp[4] describe their experiments with *Spirochæte Obermeieri.*

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(1) Centralb. Bakt., Orig., July 7, 1906.
(2) Centr. f. Bakt., Orig., June 2, 1906.
(3) Lancet, London, June 16, 1906.
(4) Jour. Am. Med. Assoc., Jan. 13, 1906.

The culture studied was obtained through the kindness of Dr. Norris, of Bellevue Hospital, New York, who secured it from a case of relapsing fever by inoculating the blood into monkeys and white rats. The organism had been kept alive by successive passage through white rats for over two months. As a result of intraperitoneal injection the parasites appear in the blood in thirty-six to forty-eight hours after inoculation, disappear within the next twenty-four hours and do not reappear. The rats are then immune to subsequent inoculation. The disappearance of the spirochæte was shown to be due to the formation of antibodies. Spirochætal blood, when kept *in vitro,* retains its virulence for more than fifteen days.

The blood of rats which have been given repeated injections of spirochætal blood exerts a most marked preventive and curative action. When injections of such blood are made, before inoculation with spirochæte, the latter fail to appear. Similarly, when simultaneous injections of immune and spirochætal blood are made, no infection results. Even when the immune blood is injected ten, twenty-four and thirty-eight hours after inoculation with spirochæte, that is to say, at any time before the spirochæte actually should appear in the blood, they will fail to appear, whereas in the controls they become numerous.

All attempts thus far to cultivate the spirochæte on blood agar have failed, but this subject will be followed further. The spirochæte multiply by transverse division and show other characteristics which belong to bacteria, notably, their behavior with reference to distilled water. When rat blood, which is rich in spirochæte, is placed in a thin collodium sac and dialyzed in running distilled water, the organisms do not undergo any change in form even after twenty-four hours. During the first five or six hours their motility is unimpaired, but after that they become more and more sluggish and finally come to rest. Even after a dialysis of eleven to twenty-four hours such blood is infective. Under similar conditions the rat and nagana trypanosomes rapidly plasmolyze, within an hour or two, and become hardly recognizable. At the same time they lose their infectiveness.

This behavior of the spirochæte in distilled water, that

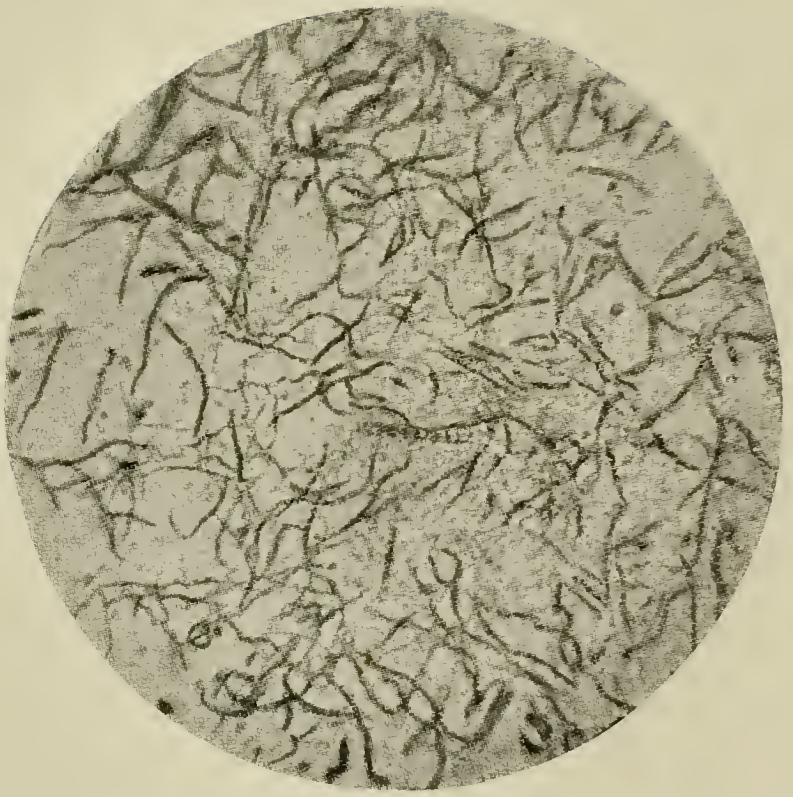
is, absence of marked plasmolysis, corresponds to that of bacteria under like conditions. This test may, perhaps, serve as a more or less general means of differentiating between bacteria and protozoa. The transverse division of spirochæte, the absence of definite structure, such as the presence of well-marked nucleus and blepharoplast, and the absence of plasmolysis would indicate that the *Spirochæte Obermeieri* belongs to bacteria.

On the other hand, the transmission of spirochætal diseases by insects, the persistence of the organisms in such insect hosts for months, and the infection of their eggs are the main facts known at present which point to a possible protozoan nature of the parasites. The persistence of the spirochæte of tick fever in the blood of rats for three to eight days, as shown by Dutton and Todd, would indicate that this organism, though closely related, is nevertheless different from that under present consideration. It goes to show that the tick fever of Africa and the relapsing fever of Europe are due to different species of spirochæte.

Protozoan Bodies in Chancre. W. E. de Korté[1] has failed to find a single specimen of *Spirochæte pallida,* although he examined most carefully a large number of syphilitics, including most of the types of secondary syphilides. Since the blood is strongly infectious during the secondary stage, it is essential that the causative agent should be recoverable in the blood at that stage, and in the course of his investigations the writer encountered a variety of bodies of protozoan nature, which he describes. While he believes that it would be too premature to speak of the causal relationship of these bodies to syphilis, the writer asserts, nevertheless, that in certain forms or phases of the disease this parasite may be found in the blood, though, for their detection, several blood smears at different times may be required, and considerable patience expended on the search.

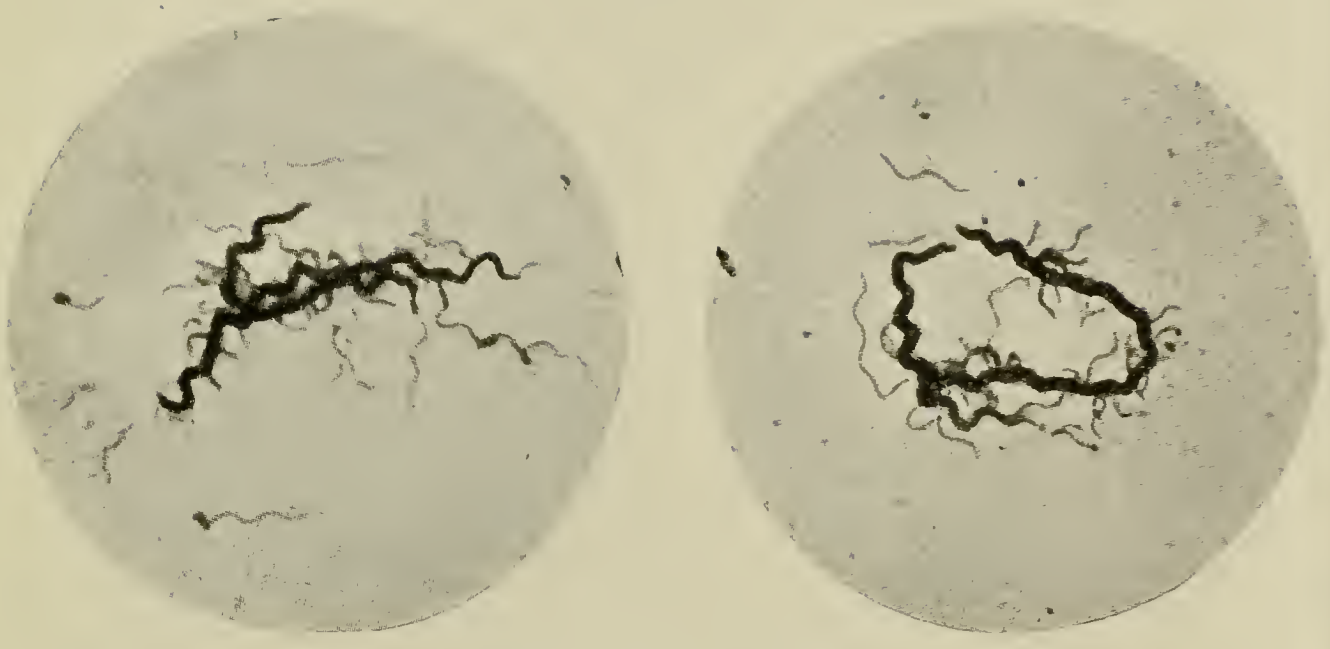
The organism takes up nuclear stains exactly like the inflammatory cells and tissue elements, and for this reason the writer experienced considerable difficulty before he was able to obtain a differential staining of the parasite

(1) Practitioner, London, June, 1906.



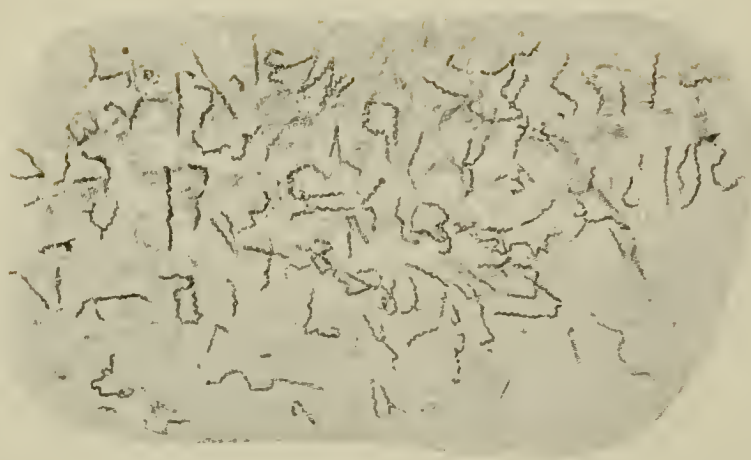
Spirochæte Dentium, 1000 :1.

PLATE VII.

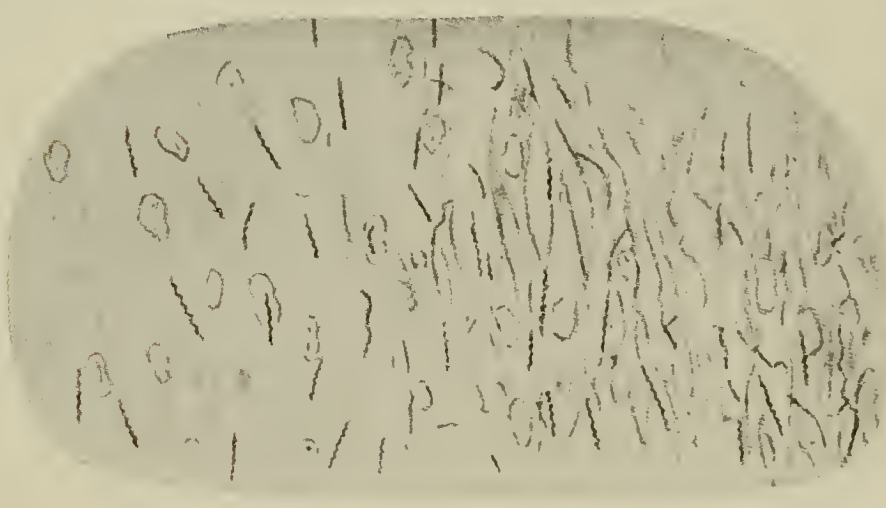


Flagella on Spirochæte recurrens, 1000 :1.

PLATE VIII.

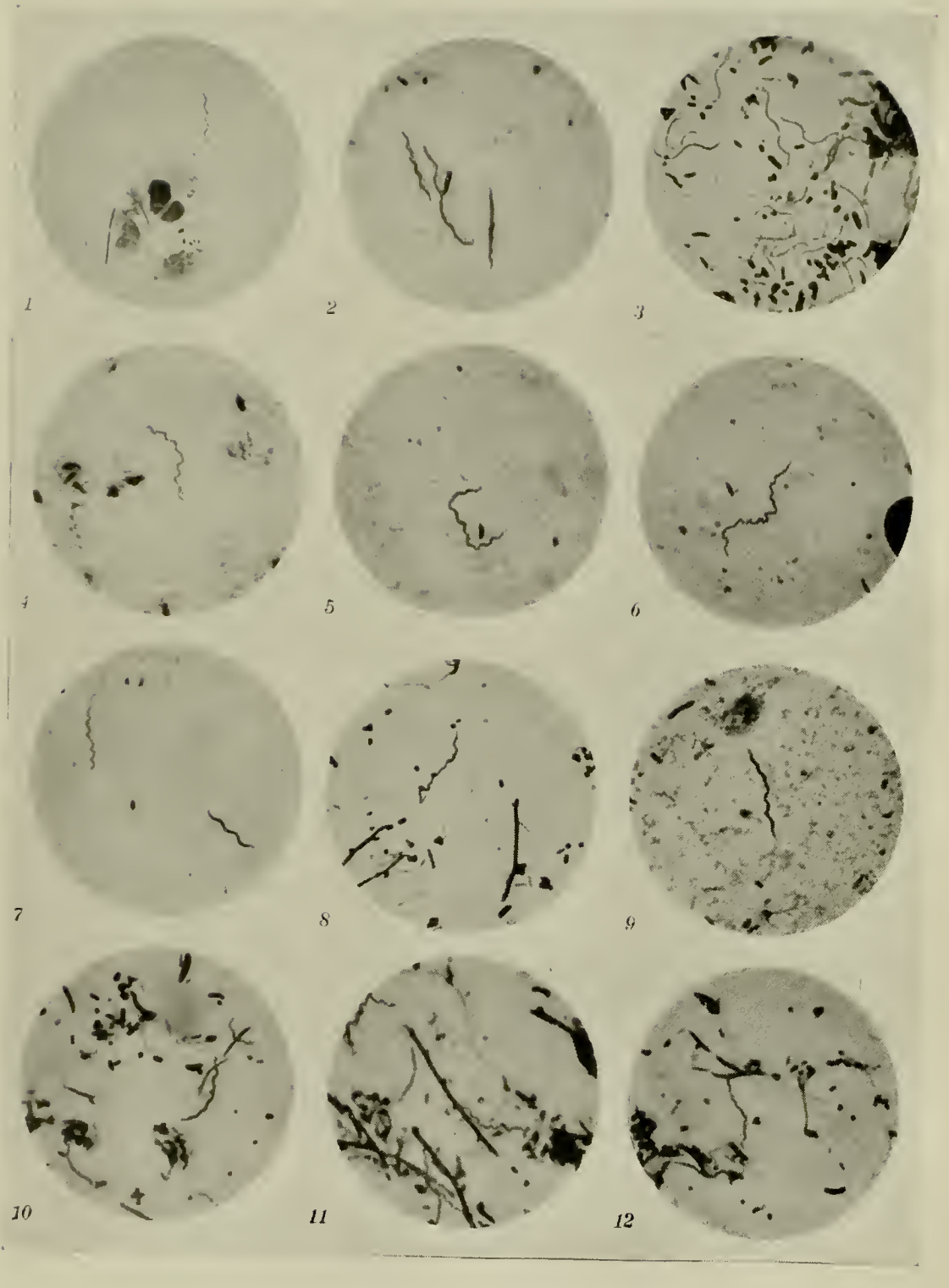


Spirochæte in a Section of the Placenta.



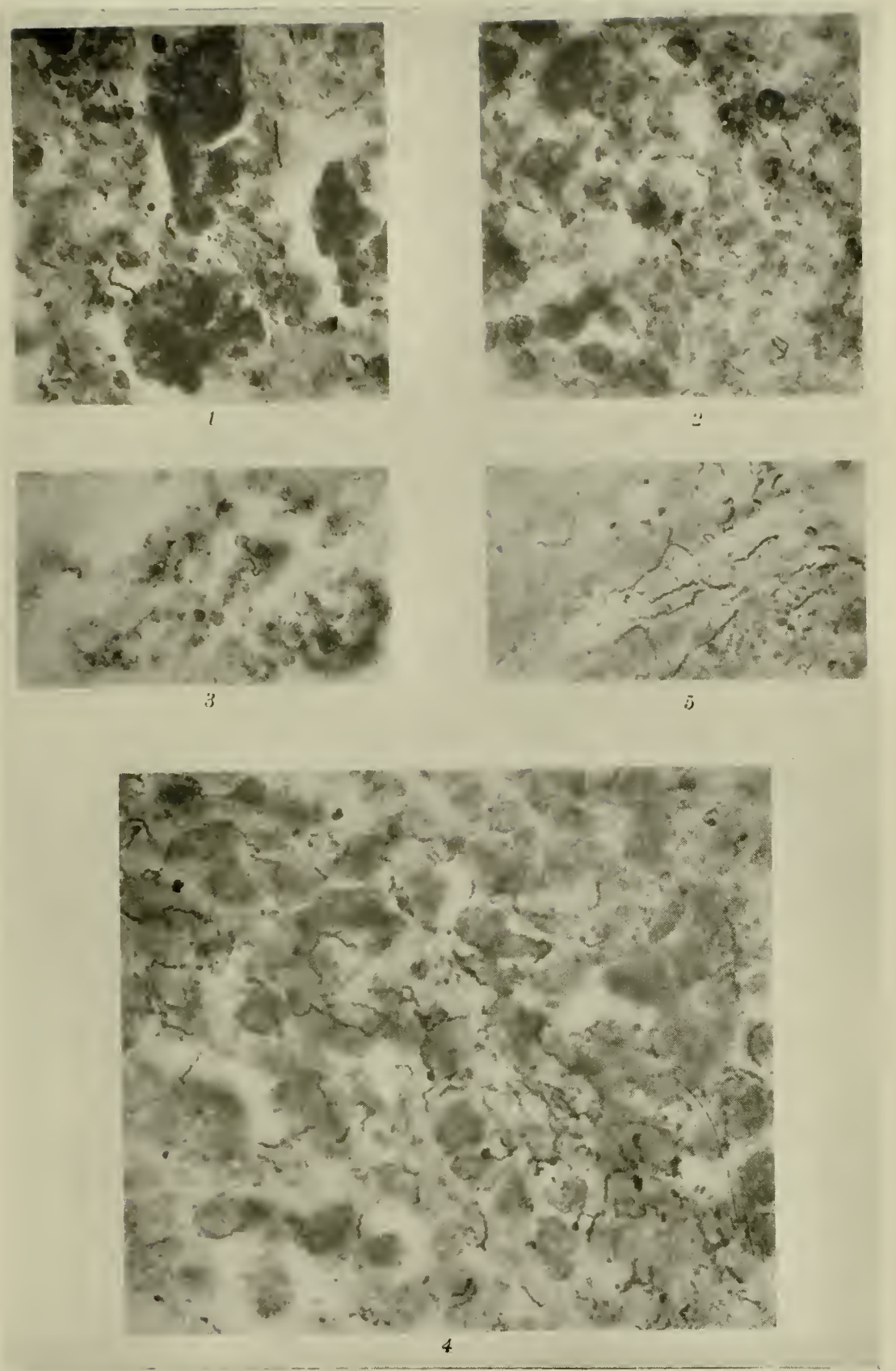
Spirochæte in the Heart Muscle.

PLATE IX.



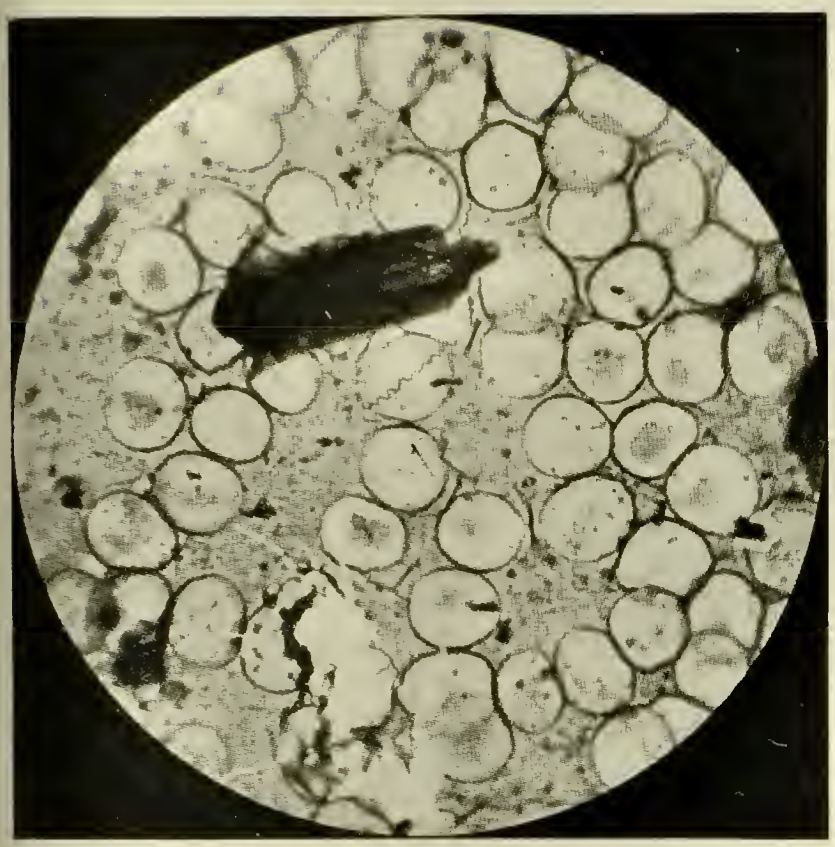
Spirochæte Pallida.

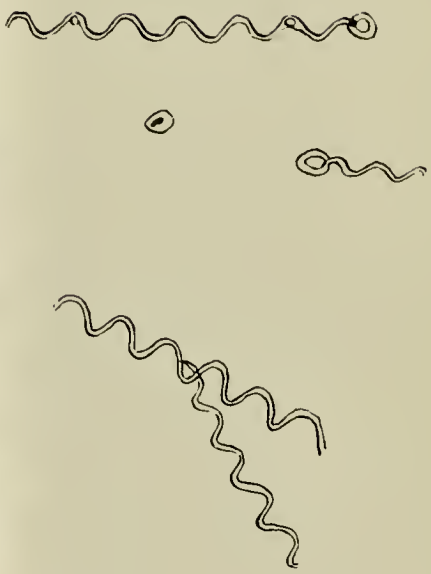
PLATE X.



Spirochæte Pallida. Nerve Fibrils Stained by Silver Nitrate Method.

PLATE XI.





Spirochæte Pallida.

PLATE XII.

in the primary chancre. The method devised needs improvement for the reason that it destroys the finer structure both of the parasite and of the tissue cells.

The infusorian has been but imperfectly studied by the writer as yet. From what little the writer has observed of the life-cycle of this organism he suggests that it belongs to the class "Ciliata."

Bacillus Tetani. *Tetanus Toxin—Eosin.* Flexner and Noguchi[1] find that eosin in solution exceeding 1.0 per cent. destroys tetanospasmin. When such modified toxins are injected into animals the symptoms which follow manifest a chronic course. The action of eosin in this way is not understood. Injections of eosin solutions were made in animals in various relations to the injections of toxin and it was found that they always modified the toxic effect, making it slower in its development and less active. When such injections were made in the immediate vicinity of injected tetanus spores the tetanus is radically modified or entirely suppressed. After tetanus toxin has been fixed by nervous tissue eosin has no effect.

The action of tetanus toxin in producing lockjaw has been investigated by Sherrington and Roaf.[2] The centers for jaw opening and closing were outlined upon the brains of orang-outang and monkeys. It was found that there is a large area, which causes opening of the jaw when stimulated and a smaller area causing closure, both located in the Rolandic area. Under the influence of tetanus injections the area of jaw opening is converted into one for jaw closing. The injection of tetanus toxin into the nerve sheath on one side resulted in lockjaw on that side for some time, but later it involved the other side as well. In the early stages the action was apparently unilateral, but by splitting the jaw it was seen to be bilateral.

Bacillus Typhi. *Conradi-Drigalski isolation method.* This procedure for the solution of *B. typhi* was fully studied by Cole[3] in 21 cases and he reports the method as satisfactory but not easy to apply. The agar with crystal violet was generally prepared following the original formula, but in the preliminary this was varied to rather test

(1) Jour. Exper. Med., January, 1906.
(2) Brit. Med. Jour., Supplement, July 7, 1906.
(3) American Medicine, March 31, 1906.

its uniformity. Bluish, non-acid colonies from plates prepared from original material were transplanted to litmus milk, glucose agar bouillon, potato and ordinary agar. When slight acidity appeared in litmus milk and no gas formation in glucose agar a further examination as to motility and agglutination tests with typhoid immune sera were made. A tabulation of the findings is appended. The method serves only to differentiate the colonies of *B. typhi* from acid producers and in this way assists the identification. Repeated examinations and an abundance of both animal and human immune sera are essential for the success of the method. The succeeding steps in the examination were as follows:

1. Transferring colonies from plate cultures prepared the preceding day to litmus milk, glucose agar, bouillon, potato, and ordinary agar.

2. Examination of cultures in the different media, Slight acidity of litmus milk and no gas formation in glucose agar required further study of the organism in the hanging drop for motility and the agglutination tests with typhoid immune sera, human and rabbit, with all motile organisms. Non-motile organisms failing to produce gas in glucose agar were tested with antidysenteric serum, 1 to 200 dilution. Those organisms which produced a slight acidity in litmus milk with a blue-green cream ring and gas in glucose agar were cultivated in fermentation tubes containing glucose, saccharose, and lactose, and the quantity of gas measured daily. Upon the third day the gas formula was taken for each organism.

3. Preparation of plates for inoculation. The method pursued was as follows: The medium was poured into plates, which were allowed to stand partially uncovered until the steam no longer condensed upon the under surface of the covers. In 15 minutes the agar had solidified and the plates were then placed (uncovered) in a dry oven at a temperature of 60° C. for two or three hours. A firm surface resulted without so much free fluid upon the surface of the plate as to prevent the development of independent colonies. If this precaution is not taken there is a tendency for the colonies to become confluent.

As less care is taken to prevent contamination of the plates during the process of pouring than is usually ob-

served, the continued high temperature doubtless attenuates or destroys many organisms which may have fallen upon the plate. Although the crystal violet inhibits the development of many of the air organisms, many more were found to develop in plates unincubated than in those incubated after having stood for a few days.

4. Inoculation of the plates: Of liquid stools three loopfuls were placed upon the surface of the medium. This material was then uniformly distributed over the surface of the medium by means of a sterile bent glass rod, turning the plates simultaneously with manipulation of the rod. The second plate of the series was inoculated by means of the glass rod being carried to it without sterilization. From the second plate the rod was carried to the third. With the amount of material used, the third plate rarely contained more than 30 to 40 colonies of all types of organisms. Of solid stool, a quantity about the size of a pea was added to 5 c.c. of normal salt solution and violently shaken until the solid matter was suspended, and then allowed to stand for 15 minutes. A series of plates was then made by taking loopfuls of the fluid and inoculating as before.

Plates were made from sputum in similar manner to the method of plating liquid stool.

Urine was centrifuged and plates made from the supernatant liquid as well as from the sediment. Definite quantities of urine were added to flasks of bouillon, and after 24 hours' incubation plates were made from these mixed cultures. Numbers of series of plates from each individual specimen were not made.

The result of the investigation is summarized in the appended chart, and serves to show the number of cases from which *B. typhosus* was isolated, as well as the appearance of cultures in litmus milk, the motility and gas production of organisms isolated from the stools, and which produced blue colonies upon lactose litmus agar. The medium serves only to differentiate the colonies of *B. typhosus* from acid producers, and in that way facilitates the identification of that organism. Success with the medium in obtaining *B. typhosus* from every case depends in a great measure upon repeated examinations, and the difficulties encountered formerly in work of this character were

only removed in the proportion which the colonies of *B. typhosus* present bear to those of acid producing organisms.

ORGANISMS.

Case.	Patient.	Number of specimens. Stools.	Sputum.	Urine.	Number of blue colonies.	Widal's reaction	Week of illness.	Morphology. Bacillus.	Coccus.	Motility.	Litmus milk. Cream ring. Blue green.	Pink.	No change.	Acid.	Alkaline.	Peptonized.	Decolorized.	Gas. Percent. Glucose.	Lactose.	Saccharose.	Formula. H.	CO_2.	Agglutination. 1 hr.—1:50 human serum.	1 hr.—1:200 rabbit serum.	Designation.
1	R. L.	8	1	2	109	+	Fourth and fifth.	+	.....	+	.....	.....	+	+	.....	.....	.....	.....	.....	.....	.....	—	.....	+	+	1 *
								+	.....	+	+	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2 †
								+	.....	+	+	.....	.....	.....	.....	+	+	+	.....	.....	.....	.....	.....	.....	.....	3
2	H. C. C.	1	.....	.....	4	+	Eighth.	+	.....	+	+	.....	.....	+	+	.....	.....	25	.....	.....	.....	.....	.....	.....	.....	4 ††
3	Unknown.	.....	.....	2	9	.....	.....	+	.....	+	.....	.....	.....	.....	+	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	5 ‡
4	C.	.....	.....	.....	10	.....	.....	+	.....	+	—	+	.....	+	.....	.....	+	86	75	5	1	2	.....	.....	.....	6 [4]
5	C. B.	9	....	1	58	+	Third.	+	.....	+	+	.....	.....	.....	+	.....	.....	20	.....	.....	3	1	.....	.....	.....	7 [5]
								+	.....	+	.....	.....	.....	.....	.....	.....	+	17	.....	....	3	1	.....	.....	.....	8
6	M.	2	.....	.....	20	.....	Fourth.	+	.....	+	+	.....	.....	+	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	2 †
7	Mr. B.[1]	12	3	7	120	+	Second to sixth.	+	.....	+	.....	+	.....	+	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	9
								+	.....	+	+	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2 †
								+	.....	+	+	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	10
								+	.....	+	+	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	10
8	P W	2	1	1	5	+	First and fourth.	+	.....	+	+	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2 †
9	H. H.	.....	.....	.....	12	.....	Third (?)	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	+	+	.....	1 *
		+	.....	—	+	.....	.....	.....	.....	+	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	12 [6]
10	M. W.	4	.....	2	24	+	Second to fifth.	+	.....	—	+	.....	.....	.....	+	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	13
		+	.....	—	.....	+	.....	.....	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	14
		+	.....	+	+	.....	.....	.....	.....	+	.....	.....	.....	+	+	.....	.....	25	.....	.....	.....	.....	.....	.....	.....	3
		+	.....	+	+	.....	.....	.....	.....	+	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2 †
		+	.....	+	+	.....	.....	.....	.....	+	.....	.....	.....	+	.....	.....	.....	30	.....	.....	3	1	.....	.....	.....	16
		+	.....	+	.....	+	.....	.....	.....	+	.....	.....	.....	+	+	.....	.....	20	.....	.....	.....	.....	.....	.....	.....	17
11	P K.	2	....	...	6	+	Third.	+	.	+	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2 †
12	Mr. B.[9]	12	.....	5	33	+	Second to sixth.	+	.....	—	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	18
		+	.....	+	+	.....	.....	.....	.....	+	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2 †
		+	.....	+	+	.....	.....	.....	.....	+	.....	.....	.....	+	.....	.....	.....	50	20	.....	1	1	.....	.....	.....	19
13	Dr G.	4	.....	5	35	+	Admitted to hospital 7-12 05. Stools plated to 7-31-05.	.....	+	—	.....	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	—	—	+	+	20 [7]
		+	.....	+	+	.....	.....	.....	.....	+	.....	+	—	+	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	6 *
		+	.....	+	+	.....	.....	+	.....	.....	.....	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	2 †
14	Mrs. M.	4	.....	4	25	?	Admitted to hospital 7-12 05. Plated 7-19 to 8-3.	.....	+	—	+	+	.....	.....	+	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	21
		+	.....	—	+	+	.....	.....	+	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	22
15	Mr. P	2	.....	2	12	+	Second.	.....	+	—	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	21
		+	.....	+	+	.....	.....	+	.....	.....	+	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2 †
		+	.....	—	.....	.....	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	23 *
16	M O	2	.....	....	10	+	Third after admission to hospital.	.....	+	—	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	24 *
		+	.....	+	+	.....	.....	+	.....	+	.....	+	-	+	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	25 *
		+	.....	+	+	.....	.....	.....	.....	+	.....	+	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	26 [10]
		+	.....	—	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	+	.....	+	.....	.....	.....	.....	.....	.....	.....	27 *
17	R. L.	3	.....	.....	12	+	Admitted to hospital 7-26 05. Plated 7-29 to 8-3.	+	.....	—	.....	.....	+	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	28 [11]
		+	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	+	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	29
18	J. M	1	.....	.....	6	—	Third.	+	.....	+	+	.....	.....	.....	+	.....	—	.....	.....	.....	.....	.....	.....	.....	.....	2 † *
19	J B.	1	.....	.....	4	—	Fourth.	+	.....	+	+	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2 †
20	M. S.	2	...	.....	5	.....	Second.	+	.....	+	.....	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	11
		+	.....	+	+	.....	.....	.....	.....	.....	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	10
21	C R.	1	...	.....	5	.....	Fourth.	+	.....	+	+	.....	.....	+	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	[12]

[1] Patient died. [2] Convalescent. [3] Litmus milk fading lilac. [4] No blue colonies appeared until urine was added to bouillon and plated the following day. [5] Decolorized in 48 hours. [6] Isolated from intestinal contents plated at time of post mortem. [7] Slate colored, fading. [8] Gas production not recorded in saccharose and lactose. [9] Slight change not markedly acid. [10] Milk slightly paler blue than before inoculation. [11] Milk slightly paler than before inoculation. [12] No blue colonies in plate; patient died.

NOTES EXPLANATORY OF TABLE.

* *B. typhosus* isolated from sputum, urine, and stool in Case 1, spleen in Case 9, and stool in Case 13. At the time of isolation of *B. typhosus* from the sputum in Case 1 the patient had a severe bronchitis.

† Represents *B. fæcalis alkaligenes*.

†† Represents *B. choleræ suis*, *B. enteritidis* (Gaertner) or *B. paratyphosus* group.

Caffein method. Birt[1] concludes from his observations as to this method of separating colon and typhoid bacilli as follows:

0.5 per cent. caffein in 1 per cent. peptone water does not always restrain the development of the *Bacillus coli communis*.

0.5 per cent. caffein in 1 per cent. peptone water in-

(1) Brit. Med. Jour., Oct. 28, 1906.

hibited the growth of twenty-six out of thirty-one strains of *Bacillus typhi abdominalis* examined.

0.5 per cent. caffein in 1 per cent. peptone water completely arrested the development of eighteen varieties of dysentery bacillus.

Caffeinated media are of service in isolating streptococci and staphylococci.

Negative results with caffeinated media cannot be relied upon to exclude the presence of *Bacillus typhi abdominalis* in water or dejecta.

Poeppelmann[1] recommends the staining of blood for typhoid bacilli as a diagnostic procedure. Blood films are made and stained by the May Gruenwald method. The bacilli are stained blue. It was generally less difficult to find the micro-organisms in specimens of blood taken in the morning, and frequently the specimens obtained at that time showed an abundance of bacilli.

A method of cultivating the typhoid bacilli from blood is reported by Fornat.[2] When bacilli are in clotted blood they die because of bactericidal action, or are caught in the fibrin network. The method used by Fornat consists in adding bile to blood or clots; this releases the bacilli and they may be cultivated. In 14 cases his results were positive before the cases gave a Widal reaction. As positive results were obtained with small amounts of blood, the method may be of practical value. Bile was obtained under aseptic precautions from the slaughter house and was used while fresh.

Czaplewski[3] calls attention to the unreliability of old litmus lactose agar in distinguishing typhoid and colon bacteria. As this medium gets older, a reduction of the indicator occurs, rendering the medium eventually useless. He suggests that litmus solution and milk sugar solution be kept on hand in sealed tubes, and at the time of making cultures these can be added to melted agar just before pouring the plates. The addition of crystal violet as recommended by some workers is not considered of value by him.

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(1) Deutsche med. Woch., No. 24, 1906.
(2) Muench. med. Woch., No. 22, 1906.
(3) Centr. f. Bakt., Bell., Abt. I, Bd. XXXVIII, Referate, 1906.

Bile cultures. Conradi[1] advocates the use of his method of bacteriologic diagnosis in typhoid by means of a bile medium. Thirty-five cases were thus examined, and of these 29 showed typhoid bacilli and 6 paratyphoid. Thirteen were in the first week, and 7 of these before a positive serum reaction. The writer's method is as follows: Ox-bile, to which is added 10 per cent. peptone and 10 per cent. glycerin, is sterilized in tubes in amounts of 10 c.c. Blood is obtained by puncturing the ear, or by aspiration from the median vein. From 0.5 to 2 c.c. is added to the bile mixture by allowing it to fall into the tube or by first drawing it up by a capillary tube. The tubes are incubated and then plates are made on agar for colonies of typhoid bacilli.

Isolation from Water. Willson[2] considers the various methods of isolating the typhoid bacillus from water and concludes that of all the methods so far proposed that of Hoffman and Ficker is most valuable. This is the caffein enrichment method. But it is advisable to supplement this process by another, so as to render the results more certain. For this purpose the writer prefers the alum precipitation method known as Schüder's method. A stock solution of alum 10 per cent. is prepared. To each liter of the suspected water 5 c.c. of this solution is added. When the precipitate has settled completely the clear liquid above is poured off and the sediment is centrifuged. The resulting sediment is spread over litmus lactose plates to obtain the suspected colonies.

Bacteriologic Examinations of the Conjunctival Sac in Typhoid Fever and in Pneumonia. Robert L. Randolph[3] employed the following method in making his cultures: Through the cotton plug of a test tube containing 1 c.c. of sterile bouillon ran a glass rod on which was tightly wrapped some sterile cotton wool; both conjunctival sacs above and below were well swabbed, care being taken not to touch the lids or lashes; then the glass rod was broken off with a pair of forceps and the swab dropped back into the bouillon at the bottom of the tube.

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(1) Centr. f. Bakt., Bilage, Abt. I, Bd. XXXVIII, Referate, p. 55, 1906.
(2) Jour. of Hygiene, No. 4, 1906.
(3) Bulletin of the Johns Hopkins Hospital, October, 1906.

Plate eultures were made not later than 15 minutes after the inoeulation of the bouillon. Aceording to the writer's findings, the bacterial flora of the saes during typhoid fever and pneumonia shows praetieally no difference from the eonjunetival flora of individuals who are in perfeet health.

Typhoid Fever Bacilli and Phagocytosis. When washed phyagocytes and typhoid bacilli are brought in contaet no phagocytosis results, but in the presence of serum the phagocytes beeome aetive. Harrison[1] eonsiders that the opsonins that cause activity of leueoeytes towards typhoid bacilli are not the same as are operative in the phagocytosis of staphylocoeci. The former he finds to be thermostable, while the latter are injured by heat. In view of this observation it is a question whether the substance in immune typhoid blood is an opsonin or the aetivity is one of simple stimulation.

Food Poisoning and Paratyphoid. This interesting subject is again discussed by Levy and Fornet.[2] Two widely differing symptom groups are observed in this condition. One, centro-nervous in origin, leads to secretory and motor disturbances; the *Bacillus botulinus* of van Ermengem with a toxin injurious to the central nervous system is aceountable for this variety. The other group of symptoms is intestinal, and the cause has been laid to the presence of a considerable number of diverse organisms: Proteus group, Colon group, *B. enteritides* and paratyphoid have been isolated from such cases.

The epidemic described by the writers occurred in a family, the members of which presented the elinical findings of typhoid fever. Cultivations from the stools of all the patients showed the presenee of paratyphoid baeillus. The malaehite-green-agar method was used for isolation. Blood cultures were made, using the bile method of Conradi, but with negative results. Agglutination tests were made with the patients' serum upon the bacilli obtained from them, and also upon a number of laboratory cultures. These tests verified the clinical study that the cases were paratyphoid. An elaborate search for the origin

(1) Jour. of Royal Army Med. Corps, October, 1906.
(2) Central. f. Bakt., Originale, May 17, 1906.

of the infection is described, but nothing positive was found. Suspicion, however, was most strongly directed towards a quantity of sausage that had been eaten.

Infusoria in Typhoid. Krause[1] describes the occurrence of flagellata in the stools of typhoid cases and describes a new species, *Balantidium giganteum*. The accompanying illustrations indicate their general appearance. The writer also calls attention to the alkalinity of stools, established through the growth of *B. fæcalis alkaligenes*, as being important for the presence and growth of these flagellata.

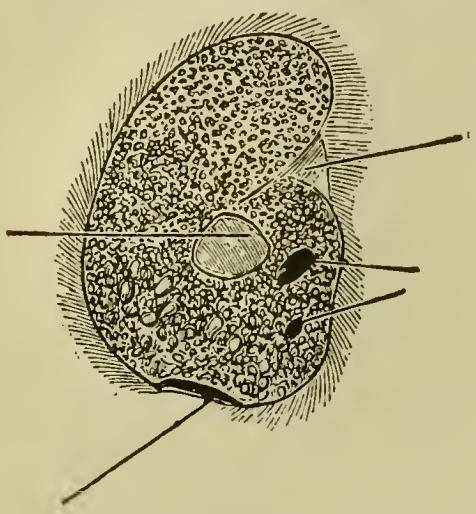

Fig. 5.

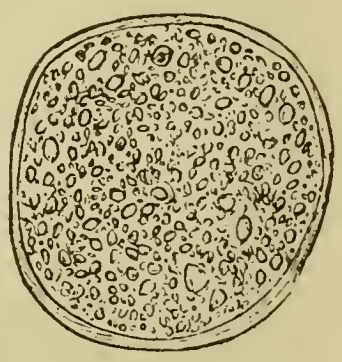

Fig. 6.

Balantidium giganteum.

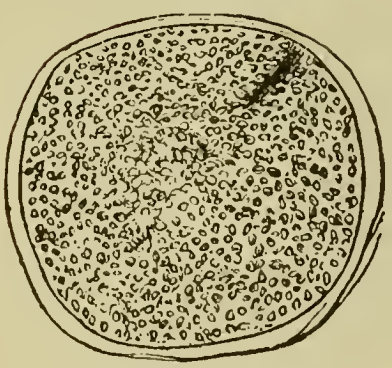

Fig. 7.

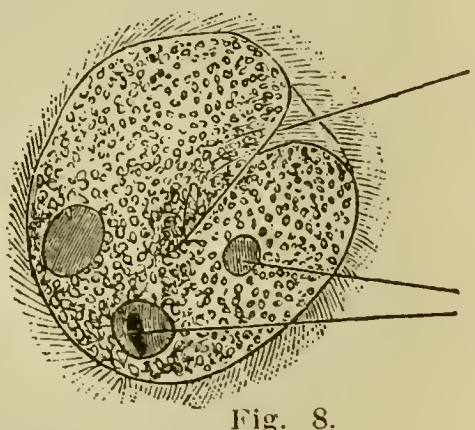

Fig. 8.

Encysted forms.

Pathogenecity of Flagellata. Biland[2] reports a case of chronic diarrhea in the causation of which the *Balantidium coli* was the probable factor. The clinical history and post-mortem findings are fully described. He fails to show any precise relation in this case, but considers that

(1) Deutches Arch. f. klin. Med., March 12, 1906.
(2) Deutsches Arch. f. klin. Med., Dec. 13, 1905.

the finding of large numbers of eosinophile cells in the intestinal mucosa points to a localization of the flagellata. These eosinophile cells are in groups, in areas or about abscesses. However, no flagellata could be demonstrated in the mucous membrane or in abscesses.

Paracolon Bacilli. *Presence in Urine.* Muir[1] describes the finding of a paracolon bacillus in the urine. From two cases of cystitis a bacillus corresponding to *B. coli* were isolated. The findings agreed with those for *B. coli* except for sugar fermentation.

The differences on this point are shown in the following comparative table:

	Glucose.	Lactose.	Cane Sugar.	Mannite	Dulcite.
B. *coli*	+	+	—	+	—
Paracolon bacillus..	A	A	—	+	—
B. *typhi*	A	—	—	A	—
Paratyphoid bacillus	+	—	—	+	+

The signs have the following meaning: + = acid + =gas formation;—=neither acid nor gas; A=acid production but no gas.

The Bacteriology of Paratyphoid. Observations on paratyphoid have been very numerous since Schottmüller[2] published his first observations on a disease resembling, clinically, typhoid, and caused by micro-organisms similar to the typhoid bacilli. The cultural methods so far known are sufficient to render possible the differentiation of paratyphoid bacilli from true typhoid bacilli, and their identification as *Paratyphus A and Paratyphus B.* Schottelius[3] has had opportunity to study a house epidemic of paratyphoid, and he endeavored to establish the value of the Gruber-Widal reaction as a test for differential diagnosis.

The cultures used at first were agar plates, and then the bacilli were transferred to bouillon. Agglutination with typhoid immune serum was absent when the dilutions were

(1) Brit. Med. Jour., Feb. 24, 1906.
(2) Deutsche med. Woch., 1900, p. 511.
(3) Muenchen. med. Woch., No. 44, Oct. 31, 1905.

greater than 1/20. The bacilli were found to differ in their cultural characteristics from the typhoid bacillus as well as from the paratyphoid of type A. The paratyphoid serum of type B gave positive reaction even in dilutions of 1/500 in ordinary temperature, as in five minutes the agglutination of the bacilli was strongly marked. Differential cultural tests also showed that the bacilli belonged to the B type.

Milk was not curdled and indol was not formed even after eight days of growth. Litmus turned at first red, then blue. Grape sugar underwent fermentation, and potato cultures showed rich, brown-yellowish colonies; on Drigalski agar the colonies formed blue patches.

Drigalski agar was found the most favorable medium for the isolation of the bacilli, and were compared after 3 to 4 days' growth with typhoid cultures simultaneously prepared; they differed from the latter by their luxurious growth. The form of growth on litmus-milk-sugar-agar described by Conradi, V. Drigalski and Jürgens as characteristic for paratyphoid bacilli of type B was observed in two instances, but could not be verified in all cases. The same is true of gelatin cultures, so that these two cannot be considered as characteristic for paratyphoid of type B. On the other hand, the milk sugar and grape sugar media and the neutral red media recommended by Rothberger and Barsickow, respectively, have been found of great value; with the aid of the latter, the two paratyphoid varieties may be differentiated from typhoid, while with the aid of the former the two varieties are differentiated from each other.

Concerning the Gruber-Widal reaction, the writer gives comparative tables showing the agglutinating power of the serum of paratyphoid patients towards typhoid and paratyphoid bacilli A and B. The differences are numerous and no definite conclusions can be drawn at the present time.

Bacillus Coli. A case of cyanosis due to *Bacillus coli* in the blood is reported by Gibson and Douglas.[1] The skin of the patient, a woman aged 36, was dark and cyanotic and she suffered for a number of years from head-

(1) The Lancet, July 14, 1906.

aches and dizziness. Blood examination showed a moderate anemia. No anatomic lesion of the circulatory apparatus was present. Cultures from the blood showed pure growths of colon bacillus.

B. Tuberculosis Toxins. The toxic properties of tubercle bacilli from which the fat was extracted by use of methyl alcohol was studied by Cantacuzene.[1] Bovine bacilli were used. A dose of 20 centigrams was found to be fatal for average guinea-pigs in 24 to 36 hours. There was a marked fall in temperature in these animals, and the blood showed eosinophilia. Smaller doses caused chronic disturbances, subnormal temperature, emaciation, tubercular abscesses and an enormous hypertrophy of the spleen. When left to themselves, the areas would disappear, and after three months the animals would recover entirely. When such bacilli were treated with iodin solution there was a great change in toxicity. They were quickly absorbed and degenerative cellular changes were not noticeable. Animals once injected with this material developed a very marked resistance to subsequent injections. The writer further noticed the stimulating effect of iodin injections upon the leucocytes and also the absorptive action that was exerted by these cells towards the bacilli and tubercular areas.

That tuberculosis is transmitted by dried sputum and dust is not considered as proved by Cadeac.[2] The change of dried sputum into dust is not an easy matter. He presents the following on this point: It took ten or twelve days for sputum dried on glass to be sufficiently altered to readily come away as dust. It persisted as a shining glazed area. When injected into guinea-pigs on the sixth day a considerable quantity was required to cause even a mild peritoneal tuberculosis. When sputum was spread on marble and dried it lost its virulence in 14 days when kept over a stove. Upon a porous plate and exposed to sunlight virulence was lost in 48 hours. When dried and maintained in the dark, virulence was preserved for longer periods, but the experimental tuberculosis produced was generally of a mild character. Tubercle bacilli mixed with sputum were often imprisoned when the

(1) Ann. de l'Inst. Pasteur, Nov. 25, 1905.
(2) Lyon Med., Dec. 10, 1905.

sputum dried. The writer contends that dust which is capable of producing tuberculosis of such mild activity when injected intraperitoneally will infect man's respiratory tract with still greater difficulty.

Baumgarten[1] discusses infection in tuberculosis with special reference to the entrance and dissemination of tubercle bacilli in the body. The difficulty of determining the point of entrance is very great, and it is only in unusual instances, as wound infections, that there is any knowledge on this point. A study of the extent and arrangement of the localized areas may give presumptive evidence, but it is always uncertain. On this account, all routes of infection are to be given consideration, and means for prevention must be directed against respiratory, alimentary or local infections.

Injections of Bacteriolysins. The direct injection into the lung of tuberculous bacteriolysins has been tried by Livierato[2] in the treatment of several cases of phthisis. The injections were generally made through the infrascapular region. In one case that is fully described the injections were made every two or three days, beginning with 1 c.c. Some 70 c.c. were given to this case during treatment. In this case the chief effect was seen in the reduction of temperature and of the amount of expectoration. Night sweats also became much less severe towards the end of the period of treatment.

Marmorek's Antituberculosis Serum. Hoffa[3] reports the results obtained in 40 cases of joint and bone tuberculosis treated with Marmorek's serum. The treatment was continued many months in some cases, but was not found to exert the least detrimental influence in any of them. Where there was extensive tissue destruction the treatment did not arrest the disease, but the writer considers that the rapid granulation that occurred in such cases is due to the antitoxin. Local irritation at the point of injection was noticed, and in some cases there was more than a simple transitory disturbance. On this account Hoffa resorted to rectal injections of serum with apparent success. The serum had a beneficial effect upon

(1) Berl. klin. Woch., Vol. XLII, No. 42, 1905.
(2) Gazz. degli Osped., Feb. 18, 1906.
(3) Berl. klin. Woch., Feb. 19, 1906.

the temperature and general condition as well as upon the local tubercular process. Roever[1] reports results of use of Marmorek's serum in 25 cases of tuberculosis. His opinion is that in surgical tuberculosis the treatment assisted in improvement and cure, but in other kinds of tuberculosis more cases must be closely studied in order to arrive at a decision. In his cases he counted the blood cells after the method of Arneth. In this method the number of nuclei in 100 neutrophile leucocytes are counted and tabulated. As an infection increases the percentage of cells with a large number (4/5), nuclei decrease. Under normal conditions the cells with four or five nuclei will number 5 per cent., and those with three nuclei 35 per cent. In disease those with two nuclei are present in increased percentage and those with four or more nuclei may be entirely absent. The course and activity of the damaging effect of the infection may be followed by this means.

Maragliano's Serum. The value of Maragliano's serum as a specific treatment in tuberculosis has been fully investigated by L. Karwacki.[2] Forty guinea-pigs and ten rabbits were used in his experiments. He found that neither Maragliano's serum nor normal serum of horse is capable of neutralizing the tuberculous endotoxins. Maragliano's serum is more poisonous for the rabbit than the normal serum of horse. It contains no antiproteins, and not only fails to protect guinea-pigs against a fatal dose of tuberculin, but it even hastens acute intoxication and death. The serum does not contain any stronger agglutinating properties than the normal serum of horse. It contains specific amboceptors and causes a bacteriolysis of the tubercle bacilli in the living organism.

The serum injected simultaneously with bacilli protects the body against anatomic tuberculosis, but does not prevent protein intoxication. Its influence upon progressive tuberculosis is unfavorable.

Denys' Tuberculin. This tuberculin has been used by Denys[3] for ten years in the treatment of all kinds of human tuberculosis. The tuberculin consists simply of a filtered broth culture of the Koch bacillus. It is free

(1) Beiträge Zur. Klin. d. Tub., Vol. V, No. 3.
(2) Zeitschr. f. Tub., Vol. VIII, No. 1, 1906.
(3) Gaz. Med. Belge, Jan. 25, 1906.

from bacilli, and the claim is made that it has not been altered by heat or chemicals, as is the case with ordinary tuberculin or the many allied preparations that have been recommended. The writer claims that his product causes a reaction in the tuberculous when given in doses of over 0.000001 gram. The injections are so gauged as not to cause a reaction. Of 442 cases of pulmonary tuberculosis 193 were cured, 56 condition good but few bacilli present, 36 greatly improved, 29 improved, 19 stationary, 9 became worse, and 100 died.

Flies Disseminators of Bacilli. Experiments have been made by Lord[1] upon flies in relation to the dissemination of tubercle bacilli. It was found that flies may ingest sputum and excrete tubercle bacilli and that these remain virulent in the flyspecks as long as 15 days. There is therefore a positive danger of tuberculosis from flyspecks on food when these are from flies that have fed upon tubercular sputum. The writer tried to infect a guinea-pig with air that was blown over such flyspecks, but found that the bacilli are not readily liberated in this way. As a matter of prevention sputum must be kept from flies and flies must be kept away from all food. Weber[2] has made a very large number of microscopic examinations of insects about cow-stalls where tuberculous cows were housed. His view that tubercle bacilli would be taken into the intestines of insects feeding about mangers and stalls was confirmed by the finding of a positive specimen. There was no evidence that the tubercle bacilli are destroyed in the intestines. In view of these findings the writer suggests that tubercle bacilli may be carried and deposited by these insects quite a distance from the barn. The infected insects may be killed in hay and may be eaten by other stock. This may happen during the period of hibernation, thereby greatly increasing the danger of infection.

Reptilian Tuberculosis. Opportunity was given Bertarelli[3] to inoculate some lizards with human tuberculosis. Cultures of bacilli resulted negatively, but sputum injections led to an infection of the animals. In one lizard the effect of inoculation was first seen in three and one-half

(1) Clin. Contrib. Mass. Gen. Hosp., Feb., 1906.
(2) New York Med. Jour., Nov. 3, 1906.
(3) Archivio p. l. Sc. Med., No. 3, 1905.

months, when the animal appeared emaciated. It was killed and a tubercular mass was found containing tubercle bacilli and giant cells. Internally the mesenteric glands were enlarged and caseous, but here no tubercle bacilli were found. The other lizard was more refractive, as after several inoculations it showed no signs of infection, and was killed. Tubercle bacilli were found at the point of inoculation, but no marked tissue changes.

Cultivation Method. The following method of cultivation of tubercle bacilli has been used by Anzilotti.[1] Pieces of potato are cut to fit test tubes and are thoroughly washed in distilled water and then boiled for twenty minutes in an alkaline 6 per cent. solution of glycerin. They are then placed in test tubes with a few c.c. of the glycerin solution in the tube under the potato. Growth appears in four or five days and continues until the potato block is covered. By this method the virulence of the cultures may be maintained for several months.

Diagnosis. Mérieux[2] reports the use of the indirect test for tuberculosis in 94 cases and states that the final outcome of the cases confirmed the tests. This test was prepared some years ago, but is little used. It consists in injecting tubercular guinea-pigs with the serum from suspected persons. The presence of reactional tubercular products causes a rise and fall in the animal's temperature similar to the effect of an injection of tuberculin. The reaction in the guinea-pig occurs 2 to 6 hours after the serum is injected. No temperature variation is noticed when healthy human serum is injected into tubercular guinea-pigs.

Agglutination. Wigham[3] experimented on two monkeys with a view of testing the diagnostic value of agglutination in tuberculosis as proposed by Arloing and Courmont. In the present report it was the writer's intention to note the agglutination action of the animals' serum from the beginning to the end of the infection. The animals were infected by feeding them human tubercle bacilli. One died in about a month, and from the condition of the lungs it was evident that the animal had previously had

(1) Clin. Med. vol. 12, No. 12. 1905.
(2) Revue de Medicine, Vol. XXVI., No. 2, 1906.
(3) Jour. of Hygiene, April, 1906.

tuberculosis. The other animal developed intestinal and miliary tuberculosis. Before feeding, both gave positive reactions in 1/10 dilution of their sera, and fair reactions up to 1/40 dilution. This condition of the serum remained practically the same during the entire period of observation. As a diagnostic procedure it was of no value.

Jessen[1] states that agglutination tests in suspected tuberculosis at 1/25 dilution is the least concentration that may be used for reliable diagnostic results. He reports tests on 86 patients and found that the agglutinating power increased after arrival at the elevation of Davos. Patients under tuberculin treatment showed no increased agglutinability. As recovery progressed the reactions became stronger, but they sank again when recovery was clinically established.

Smegma Bacilli. Mezincescu[2] describes a case in which smegma bacilli were found in a tumor on the cheek. The diagnosis of epithelioma was established and the suspicious bacilli were differentiated by their failure to retain the fuchsin stain when treated with 95 per cent. alcohol. A careful study of reactions from the growth further showed that the bacilli were almost entirely in the upper layers of the skin, and especially about the hair follicles. The number present and their arrangement pointed against the possibility of a tubercular infection. The identity of this bacillus with the bacillus of Lustgarten is now generally accepted. In a case having the peculiarities of the one described, the conditions are excellently presented upon which earlier observers would have made a diagnosis of syphilis. Further, it is an instance where it is necessary to use the most careful technique in order to arrive at a decision.

[Animal inoculations should have been made in this case. Although the writer has clearly presented his findings and the reasons for his diagnosis, still it must be considered as a serious oversight upon his part not to have determined the pathogenicity of the bacilli in the case.—Ed.]

Bacterium of Whooping Cough. Bordet and Gengon[3]

(1) Beitr. z. klin. d. Tub., Vol. VI, No. 2, 1906.
(2) Deutsche med. Woch., Nov. 30, 1905.
(3) Le Scalpel, Sept. 2, 1906.

describe an organism that, they consider, is the etiologic factor in whooping cough. The organism is abundant at about the fifth day of the disease. The expectoration, which contains large numbers of leucocytes, generally shows a great mixture of micro-organisms, among which influenza-like bacteria may be seen. The bacterium described by the writers differs from this organism, however, in that it is more regular and ovoid in shape, it grows well on media without hemoglobin, and the colonies are whiter and thicker. It does not grow on ordinary media, and therefore differs from previously described whooping cough bacteria. The writers consider the organism found by them as the cause of whooping cough, because it is present in the leucocytic secretion expectorated at the height of the disease. The bacteria are sometimes present in nearly pure culture. The blood of children shows marked agglutinating properties toward this organism for some time after recovery from the disease. Before the attack agglutination tests are negative.

The bacterium described is very small, even ovoid in form, and stains poorly with ordinary stains. It is asporogenous. The most suitable culture medium is defibrinated blood pus gelatin and glycerin. Dog serum is also a suitable medium. Upon the first cultures very slight growth is apparent, but in subcultures a thick, whitish growth is obtained.

Yellow Fever. Further observations on *Stegomyia fasciata* and yellow fever transmission are reported by Marchoux and Simond.[1] The investigation described deals with the passage of the causal agent of the yellow fever from the parent mosquito to the young. Earlier experiments had failed to give definite results. The experiments were begun with a female stegomyia, which was allowed to bite a patient with a moderate attack of yellow fever. A few days later she deposited a batch of eggs. These were hatched, and later two females were selected and fed artificially for some time. A Portuguese, who had not had yellow fever, was now allowed to be bitten by these mosquitoes, but with a negative result. Eight days later he was again bitten by one of these mosquitoes.

(1) Ann. de l'Inst. Pasteur, January, 1906.

Four days later yellow fever infection was manifest, and the attack, although mild, was in every way typical. The patient recovered and was later experimentally bitten by mosquitoes which had been infected from yellow fever patients. His immunity apparently was complete. This transmission to the young may be the cause of recurrence of yellow fever after an epidemic is apparently suppressed. The writers further found that water containing infected dead mosquitoes would not infect larvæ being reared therein, nor were they infected by the dejecta or vomit material from the second stage of the disease. On lowering the general temperature to 20° C., the mosquito apparently lost the power of transmitting yellow fever.

A series of papers on yellow fever by Marchoux and Simond[1] describe their studies on the dissemination of this disease. Some of their observations upon the mosquitoes are worthy of notice. *Stegomyia fasciata* is the transmitting agent. These mosquitoes are infected by biting patients during the first three days of the disease, and are then able to infect susceptible persons after a period of twelve days has intervened. The writers observed that the ability to infect persons may be transmitted by the female to the young hatched from eggs laid after the twelfth day. It required that a period of fourteen days should elapse before the adult young mosquitoes showed infective powers. Patients in the incubation period were never able to infect mosquitoes. During the night one is in danger of being bitten by these mosquitoes, while from 7 a. m. to 5:30 p. m. the writers believe that outdoor occupations can be pursued without fear. Stegomyia was not found to die after depositing its first group of eggs, but it lays seven batches and its life duration as an adult is 20 to 30 days. The fact that the female continues to live after the eggs are deposited is an important factor in mosquito transmission because of the necessary 12-day period of incubation of the virus in the infected mosquito. Most species of mosquitoes die at about the eighth day of adult life, or shortly after the eggs are deposited.

(1) Ann. de l' Inst. Pasteur, March, 1906.

DIAGNOSTIC METHODS.

Biologic Diagnosis of Infectious Diseases. The possibility of using the precipitin method of identifying albumins in the diagnosis of infections is receiving some attention. The presence of this phenomenon in tapeworm infections is indeed established. Bruck[1] considers the subject at length. The basis of these diagnostic tests depends upon the presence of specific bodies in the blood serum of the patients. Owing to the presence of antibodies, there are a number of diseases in which the method is now of extreme importance. The determination of the presence of antibodies is an indirect method, because the test as a Widal reaction only develops as an after effect due to the presence of typhoid bacillus. Our direct methods are by microscopic and cultural examinations—to which the addition of the chemic biologic method would be a most acceptable adjunct. There are present three bodies: the specific albumin, the antibody, and the complement. The writer showed previously that when two are known it is possible to determine the third in proper mixtures. It is this fact that may open the way to diagnostic procedures. Along the lines of diagnosis in tuberculosis and syphilis, some promising investigations have already been reported.

Bruck's remarks in the present paper are upon serum diagnosis of miliary tuberculosis. Heretofore the finding of tubercles in the eye and cultivation from the blood have been the only certain diagnostic methods. It has been shown that dissolved tubercular substance cannot be demonstrated in the blood serum of consumptives, nor can antituberculin be demonstrated in these cases before they have been treated with tuberculin. In military tuberculosis there should be a difference from these findings. As the bacilli are disseminated throughout the body, it is quite positive that a certain amount of dissolved material from

(1) Deutsche med. Woch., June 14, 1906.

the bacilli is also present. At the same time, it might be expected that antibodies to the tubercular material would be spontaneously produced. The patient is overwhelmed and dies if this mechanism is not sufficiently active to overcome the infection. The serum tests for these two substances were made upon a case of miliary tuberculosis.

The test for the presence of tuberculin bodies in the patient's serum was made as follows: Blood was obtained by vein puncture and then centrifuged. The clear serum thus obtained was heated to 55° C. for 30 minutes. Equal quantities of a high grade tubercle immune serum were mixed, with decreasing amounts of the patient's serum, and also equal quantities of fresh normal guinea-pig serum (complement). The mixture remained in the incubator for one hour. There was now added twice the amount, to cause complete laking of an inactive hemolytic serum, and a 5 per cent. dilution of the corpuscles of the species used in preparing the hemolytic serum. The complete mixtures were placed in the incubator for one to two hours, and then on ice over night. At the same time control tests were made, as shown in the table:

Test for Tubercle Bodies in Patient's Serum.

	Tubercle Immune Serum.	Patient's Serum	Fresh Normal Guinea-pig Serum	Inactive Rabbit Serum Immune to Cattle Corpuscles	5 Per Cent. Cattle Corpuscles.	Result
Tests	0 1	0.1	0.1	0.0002	"	Partial Laking
	0.1	0 05	0 1	0.0002	"	do
	0 1	0.01	0 1	0.0002	"	Complete Laking
Control	0.1	—	0.1	0.0002	"	Complete Laking
	—	0.1	0.1	0.0002	"	do
	—	—	0.1	0.002	"	do
	—	—	0.1	—	"	0
	—	—	—	0.002	"	0

Later in the course of these cases similar tests gave a negative result; that is, the hemolytic or laking action was not affected. Tests along the same lines were then made, as shown in the accompanying table, to determine if antituberculin bodies had been formed. It appears from this that such was the case.

TESTS FOR ANTITUBERCULIN IN PATIENT'S SERUM.

Patient's Serum.	Old Tuberculin	Fresh Normal Guinea-pig Serum.	Inactive Rabbit Serum Immuns to Cattle Corpuscles	5 Per Cent. Cattle Corpuscles.	Result.
0.1	0.1	0.1	0.0002	"	Partial Laking
0.1	0.05	0.1	0.0002	"	Complete Laking
0.1	—	0.1	0.0002	"	do
—	0.1				

THE BLOOD.

Viscosity of Blood. Ditermann[1] shows a modification of the Hirsch-Beck apparatus for determining the viscosity of the blood. As shown in the cut, the instrument consists of a small, graduated, bent tube. The connecting tube is filled from an ear puncture to the mark .275 c.c.

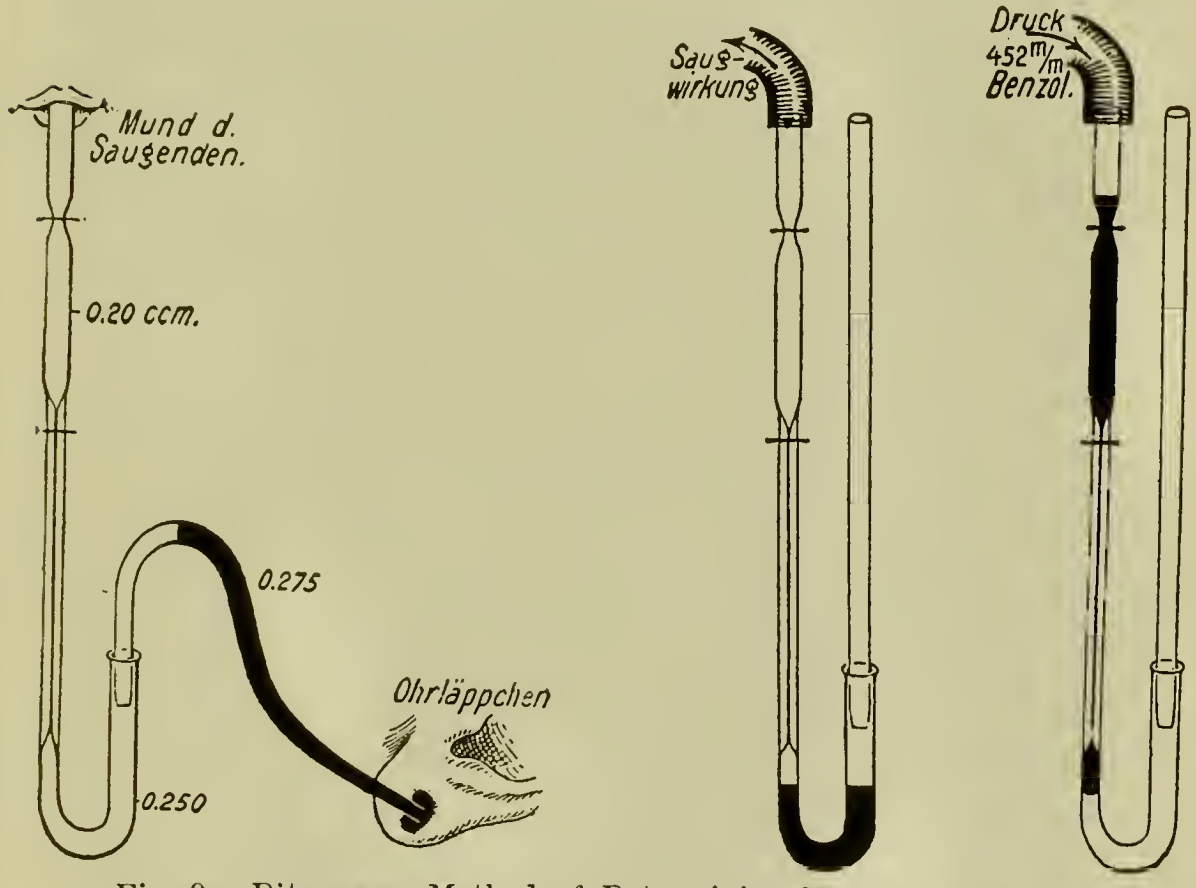

Fig. 9. Ditermann Method of Determining Viscosity of Blood.

To prevent coagulation of the specimen taken, a very small amount of hirudin is placed on the skin at the point of puncture, and the exuding blood comes sufficiently in

(1) Muench. med. Woch., May 8, 1906.

contact with it to insure thorough mixing. The blood is now drawn into the long arm of the tube to the graduations, and held in place by the glass stopper that is inserted into the lower open end of the U tube. Next the upper end is connected with a column of benzol of 452 mm. The observations are made by taking the time necessary for the blood to flow through the capillary opening in the tubes. For distilled water this is 6 to 8 seconds and for blood 30 to 40 seconds. The apparatus should be warmed to a degree close to the temperature of the normal body.

Bilirubin in Blood. Biffi[1] describes his test for bilirubin in the blood as follows: From 2 to 5 c.c. of blood are obtained, and to it is added a small amount of sodium oxalate, to prevent coagulation. The blood is now extracted by shaking with about two volumes of chloroform and then filtered. The chloroform appears in the filtrate and shows a bright yellow or orange tint when bilirubin is present. If large quantities of blood are taken and the filtrate concentrated, it can be shown that bilirubin occurs in normal blood.

Test for Blood. Robertson[2] reports his personal experiences with the Uhlenhuth serum test for blood of different species of animals. The usual procedure for this method was used by the writer. The specimens used were from a few weeks to 9 years old. In the case of older specimens the reaction, as shown by the precipitate, took place more slowly. Fig. 10 illustrates the result.

Typhoid Blood Cultures. Muller and Graef[3] find of great advantage the use of hirudin (bile extract. Sachse & Co., Leipzig) to prevent coagulation of blood in testing for typhoid bacilli. A solution of 0.01 gm. hirudin in 2.5 c.c. normal salt solution is sufficient to prevent 75 c.c. of blood from coagulation. Such mixtures may be kept for a number of days without coagulation. If kept quiet, the corpuscles settle and there is a clear plasma. Blood specimens can be drawn into tubes from veins, or the ear, and directly mixed with the contained hirudin solution when they are safe to be taken to the laboratory and exam-

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(1) Bull. delle Sci. Med., May, 1906.
(2) Scottish Med. and Surg. Jour., April, 1906.
(3) Muench. med. Woch., Jan. 9, 1906.

ined by cultures several days later. Any method of culture may be used.

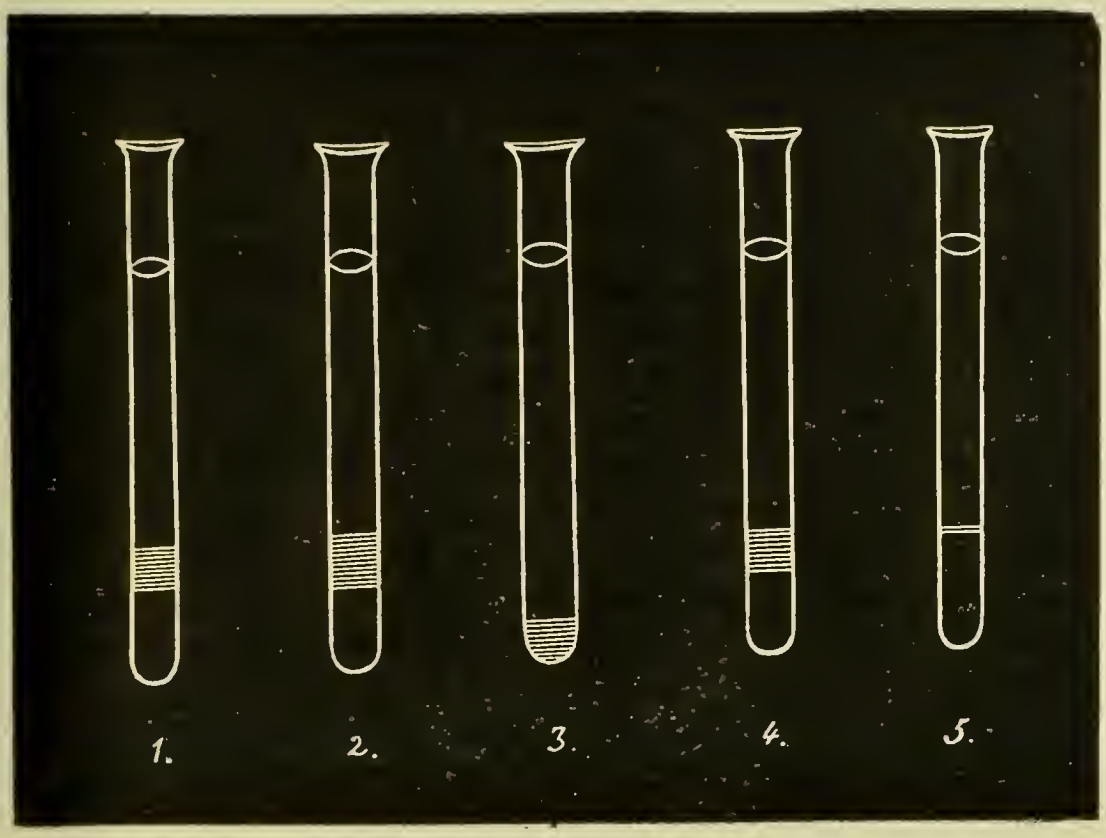

Fig. 10. Robertson's Tests.

1. Reaction with solution from a blood stain 4 weeks old, after 5 seconds.
2. The same after 12 seconds.
3. The same after 30 minutes.
4. Reaction with stain 9 years old, after 10 minutes.
5. No reaction with blood of ox.

Experiments with Blood Cultures. The paper by Libman[1] deals with blood cultures in bacterial infections. When bacteria attack any part of the body the local lesion is termed a local infection. If the lesion is one that can not be diagnosed it would be termed a cryptic infection. When bacteria are present in the blood it is a bacteremia or systemic infection. In these conditions metastatic infections may occur. If the point of infection in these blood localizations is not known the condition would be termed a cryptogenetic bacteremia. In distinction from bacteremia a septicemia generally is reserved for conditions where the bacteria multiply in the blood. In secondary infections one bacterial infection follows another.

(1) Johns Hopkins Hospital Bull., July, 1906.

An intercurrent infection is one that appears during the course of a nonbacterial disease. In mixed infections several varieties of bacteria are present. When the blood is involved in mixed and secondary infections the terms secondary bacteremia and mixed bacteremia may be used. Agonal invasions take place just before death. Terminal infections may be the cause of fatal termination in chronic diseases, or the term may be used to designate the infection present at the time of death.

It is desirable to use a variety of media in investigations of this kind, and to use both solid and liquid media. The average amount of blood to be used is 25 c.c. When typhoid is to be looked for the blood is diluted, and when streptococci or other pus cocci and pneumococci, it should be used in concentrated form. Of the solid media, glucose serum media are the most satisfactory, while glucose bouillon often gave results where other liquid media failed. The accidental contamination of cultures demand special care and should be fully investigated.

Pneumococci are to be identified by their capsules, fermenting inulin; streptococci by precipitating (whitened) growth on serum-glucose-agar, and hemolysis on blood-agar plates; gonococcus, by being Gram negative. Cocci must be very carefully studied before pronouncing them gonococci, even if there is failure to cultivate them. In the case of staphylococci, six or seven days must be allowed for color production, and potato medium should be used. A general summary of the results of some 700 blood cultures is introduced. It is specially interesting to note that cultural experiments in cases of acute leukemia gave only negative results, and when bacterial growths were obtained they were found to be accidental. When blood cultures are negative the infection may not be by the ordinary bacteria, but may be due to tuberculosis, actinomycosis, syphilis, or protozoa. The bacteria may be localized or not in the blood, or they may have disappeared from it. An embolus may pass through the blood stream without giving rise to a bacteremia.

If bacteria are found and the primary focus is treated they may disappear slowly or rapidly. With or without treatment of the primary focus, the bacteria may remain in the blood, metastatic foci or endocarditis may or may

not develop. In some instances after secondary foci are established the bacteria disappear from the blood stream. Bacteremia may result from surgical intervention or extensive handling of an infected focus. The patient may recover even when a relatively considerable number (500 colonies of *Micrococcus aureus* to the c.c.) of bacteria may be present in the blood. When bacteria are present in fairly large numbers in the blood they are usually found in the urine.

Quinin as a Test for Blood. Horoszkiewicz and Marx[1] find that when hemoglobin is treated with quinin the spectroscope will give a characteristic spectrum between the C. and D. lines. Old stains or clots show as well as those from recent specimens. The spectrum can be readily seen by taking four parts of a 10 per cent. quinin solution and two parts of blood and heating the mixture. The presence of CO in blood can also be shown by mixing the blood and quinin solution as above and heating to boiling, over a burner. When somewhat cool a few drops of ammonium sulphate solution are added. A carmine color appears if carbon monoxide is present; when absent the color is greenish brown.

THE STOMACH.

The Sahli Test. Alexander and Schlesinger[2] find that the unreliability of this test lessens its value. In some cases of minimal secretion the test was positive, and in others with normal functions it failed. The results are based on a study of 48 cases.

Digestive Tests. Einhorn's method[3] consists in filling the holes in glass beads with foods of different kinds. The beads are recovered from the feces and examined for the action on the food material. The digestibility of various substances may also be learned by these tests. When the stomach functions are to be tested the beads are withdrawn at the desired time by means of a thread attached

(1) Berl. klin. Woch., Vol. XLIII, No. 35.
(2) Deutsche med. Woch., No. 22, 1906.
(3) Med. Record, Feb. 10, 1906.

to them. The writer goes on to describe the results upon a large number of food particles, both in the stomach and in the intestines. When the beads are placed in gelatin or other capsules they can pass the stomach and show only the result of intestinal digestive activity.

Milk Tests. Whitman[1] describes a new milk-testing bottle of his own design, which should be of interest not only to milk laboratory workers but also to physicians.

Its advantages consist in greater accuracy; more compact form, making its use available for smaller quantities of the fluid, as in testing human milk; and its saving of the expense of the special centrifuge necessary for the regulation Babcock bottle.

The Whitman bottle is about 3.75 inches long, and of the shape to fit the ordinary aluminum centrifuge sheath. It is marked at three points, indicating respectively 2.5, 5 and 10 c.c. These make it possible to get along without the corresponding volumetric pipettes. Into the neck of the bottle is ground a glass tube of such length that, when inserted in the bottle, bottle and tube measure not more than 5.5 inches in length, and the sheath must be long enough to allow the bottle to swing free in the jaws of the centrifuge arm. This tube is calibrated to hold 0.25 c.c. (i. e., 5 per cent. of 5 c.c.), which is divided into five major divisions, and each such major division is again divided into five parts.

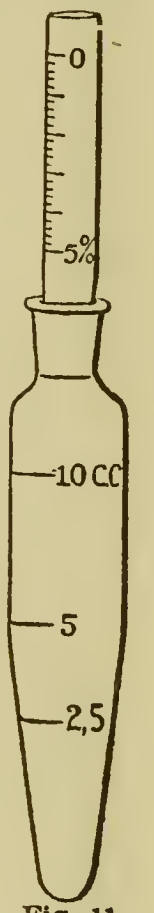

Fig. 11. Whitman Bottle.

Bottles designed for testing cream have a tube calibrated to hold 0.75 c.c. (i. e., 15 per cent. of 5 c.c.), subdivided in the same way, so that each major division corresponds to 3 per cent. of fat when 5 c.c. of cream is used in making the test, and to 6 per cent. when 2.5 c.c. is used. A stout string tied about the neck of the bottle, and reaching beyond the sheath, will be found convenient in drawing the bottle out of the latter after use.

Technic.—To test milk proceed as follows: Fill the

(1) Bulletin Chicago Health Department, 1906.

bottle with milk to the mark 5, and then with sulphuric acid, sp. g. 1.82-1.83 (91 per cent.), to the mark 10. Mix carefully, being careful that the hot mixture does not spill on the hands or clothes. Place the bottle in the sheath and centrifugate for two minutes at a reasonably high speed. A power centrifuge, of course, is convenient, but by no means necessary. Remove the bottle from the sheath and fill it to the base of the neck with hot water, insert the tube in the neck, and fill the latter to the top of the calibrated portion with hot water by means of a dropper with a fine point. Place the bottle in the sheath again, and recentrifugate for one or two minutes.

On removing the bottle from the sheath to take the reading it will often be found that the column of fat has sunk so low in the neck, from cooling, that a reading can not be taken. If this is the case, set the bottle for a few seconds in a dish of hot water, watching it until the column of fat rises well into the tube, when the reading may be taken. In case the fat settles to a point below the lower end of the tube, a part of it may fail to enter the tube again when it is heated.

One can easily protect himself, and if necessary correct any errors from this source, by the following simple procedure: After taking the first reading, place the finger over the upper end of the tube so as to close it, and remove the tube from the bottle. Discard the contents of the tube, wipe out the latter, return it to the bottle, and again fill it to the upper end, as before, with hot water; now centrifugate again, and add any fat thus found to the fat obtained in the first reading.

For testing cream, the method is identical, except that the larger calibered tube is used. For creams containing above 15 per cent. butter fat, the bottle will not give a reading if 5 c.c. of cream is used. In this case, fill the bottle with cream to the mark 2.5, then with water to the mark 5, and finally to the mark 10 with acid, and proceed as before.

The following table, modified from Holland's "Medical Chemistry and Toxicology," will be found useful in judging the quality of the sample of milk:

Milk	Sp. g.	Percentage of butter fat.	Proteids and Quality
Normal average.....	1.031	3.5	
Healthy variations....	1.028—1.029	4.5-6	Normal (rich milk)
" "	1.0s2—1.033	2.5-3	Normal (fair milk)
Unhealthy "	Below 1.028	Above 5.0	Normal or slightly below
" "	" 1.028	2.5-5	Low (poor)
" "	" 1.028	Below 2.5	Very low (very poor)
" "	Above 1.033	Above 5.0	Very high (very rich)
" "	" 1.033	2.5-5	High
" "	" 1.033	Below 2.5	Normal or nearly so

Feces. *Gram Stain of Stools.* Elliott[1] used the Gram staining method in 25 gastro-intestinal cases; 16 were negative, 7 positive and 2 mixed. In consideration of the possibility of carcinoma in these cases it was found that among the 16 cases with negative Gram stool one showed carcinoma, while among the 7 with positive Gram stools one had gastric ulcer, the other six carcinoma. The writer considers the test can greatly help in the differentiation of intestinal carcinoma from diseases of other structures. It is also of value in the continuous observation of patients with old gastric ulcers, as in such cases it may help to determine the time of appearance of carcinoma.

Tissue. *Romanowsky's Stain.* May[2] modifies the Romanowsky staining method as follows: First stain with acid eosin methyl blue solution in 25 per cent. strength in wood alcohol. Wash quickly in distilled water and without drying. Stain with 0.5 per cent. methylen azur solution. The writer often observes the staining effect taking place under the microscope and stops it by again washing in distilled water. In this manner no precipitates are formed. This stain is also useful for blood specimens where a differential count or examination for blood parasites is desired.

Triple Staining of Tissue. Bonney[3] gives the following method for the triple staining of sections of tissue:

Technique.—1. Fix small pieces of the tissue in acetic alcohol. (The fixatives of Hermann and Flemming may be used if preferred. The older and inferior fixatives such as alcohol, etc., are useless as regards the fine details for

(1) Chicago Med. Recorder, June, 1906.
(2) Muench. med. Woch., Feb. 20, 1906.
(3) Lancet, London, Jan. 27, 1906.

which this process was devised, whilst formalin renders it impossible of performance.) 2. Embed, cut, and mount in the usual manner. 3. Stain for one hour in a saturated watery solution of saffranin. 4. Wash in water. 5. Stain for a quarter of an hour in a saturated watery solution of methyl violet. 6. Wash in water *and wipe the slide dry except that part occupied by the section.* 7. Have ready in a drop-bottle the following solution: to 20 c.c. of acetone add *drop by drop* a saturated watery solution of orange G. until the flocculent precipitate, which slowly appears, on shaking is just dissolved in excess of the watery solution; then filter. 8. Flood the slide with this solution. A cloud of color immediately comes out which obscures the view of the section. 9. Pour this off on to blotting-paper and flood again with the same solution. The color cloud being much fainter the section can be watched. 10. When the section has attained a *rather faint* brownish-pink color, pour off the orange-acetone solution. 11. Wash in acetone for a few seconds. (*This should be continued in a small glass jar. Acetone being very volatile, care should be taken that the section does not dry.*) 12. Wash in xylol. 13. Transfer to low-power microscope and see if the proper result has been attained. 14. Wash in two fresh changes of xylol. 15. Mount in xylol-balsam.

Result.—All chromatic elements, nucleoli, and certain nuclei, such as those of polymorphonuclear leucocytes, stain a rich violet, chromosomes standing out with peculiar distinctness. The spindle fibers of nuclear mitosis stain a faint pink. The cytoplasm stains a rose pink. The intercellular tissue stains a pale yellow. These effects are best seen if the slide be examined through a deep blue screen.

Method of Preparation.—Wilson's[1] rapid method of preparing fresh tissues for the microscope is as follows:

Bits of fresh tissue not more than 2x10x10 mm. are frozen in dextrin solution and cut in sections of from 10 to 15 microns thick.

The sections are removed from the knife with the tip of the finger and allowed to thaw thereon.

The sections are unrolled with camel's-hair brushes in 1 per cent. NaCl solution.

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(1) Jour. Am. Med. Assoc., Dec. 2, 1905.

The sections are stained from 10 to 20 seconds in neutral Unna's polychrome methylen blue.

They are washed out in 1 per cent. NaCl solution.

They are mounted in Brun's glucose medium.

The microtome used is the Spencer automatic with a CO_2 attachment in which vulcanite is substituted for brass in the wall of the freezing chamber, thus insulating the freezing plate.

The Urine. *Acetone.* Frommer[1] presents the following test for acetone: The urine is made strongly alkaline with potassium hydrate and a few drops of a 10 per cent. solution of salicylic acid in alcohol are added. The mixture is heated to 70° C. In the presence of acetone a purple red ring will appear in the lower portion of the fluid.

Quantitative Testing. Bluth[2] describes the following method for the quantitative estimation of acetone in the urine: The principle involved in this method depends upon the delayed color reaction when greater amounts of acetone are present. When sodium nitroprussid is added to acetone containing urine and followed by sodium hydrate and then acetic acid a play of colors occurs, beginning with red and changing to yellow. The time intervening from red to yellow has been used by Bluth in his quantitative determinations. In conducting the tests 20 c.c. of urine are treated with 2 c.c. zinc chlorid solution (equal weights zinc chlorid and distilled water), shaken and filtered to give exactly 15 c.c. of clear filtrate. To this is added 1.5 c.c. lead acetate, and then it is shaken and filtered to give exactly 7.5 c.c. of clear filtrate. This filtrate is mixed with an equal quantity of sodium hydrate and again filtered if necessary. Of this mixture 10 c.c. are taken and are poured into a test tube that contains 1.5 c.c. sodium nitroprussid. Instantly the red color of the reaction is seen and the time must be taken as the color gradually changes to orange, greenish-yellow and canary yellow. It is best to use a comparison color prepared by mixing two parts liquor ferri sesquichlorid and one part distilled water. When this color is matched the time is noted. In normal or acetone free urine the time for the

(1) Berl. klin. Woch., Aug. 7, 1905.
(2) Deutsche med. Woch., Jan. 25, 1906.

change to occur is about 20 seconds. A comparative test can be made using the same urine if it is first thoroughly boiled and then brought back to volume and carried through as described. In the presence of acetone the time for the matching of the colors is delayed and each second of delay equals 0.01 gram of acetone per liter. Five seconds equal 0.05 gram acetone and 200 seconds 2.0 grams per liter. This method has been shown to be as reliable and as exact as the distillation method. There is only one condition in which it cannot be used and that is when the urine contains diacetic acid as well as acetone. The writer promises to report further in regard to this matter.

Test for Indican. Gruber[1] tests for indican in the urine by means of osmic acid. To some urine in a test tube a double quantity of strong hydrochloric acid is added, and followed by 2—3 drops of a 1 per cent. osmium solution. The mixture is shaken. Almost immediately the urine turns to a violet color if indican is present, and then, according to the amount, to a blue-violet or blue color. If the osmium solution should be in excess it does not injure the test. The indigo blue may be removed by shaking with chloroform as in the Obermayer test. Concentrated or highly colored urine should be clarified with lead acetate.

Sugar. *Haines' Solution.* Simroch[2] describes and advocates Haines' solution (written Heinsche Loesung) for sugar testing. He says it is generally used in some of the clinics in preference to other reagents and is as delicate as the nitropropiol-tablets which are now widely used in Europe.

Pedersen[3] uses an eye dropper for making ring or contact tests for albumin in urine or other fluids. The dropper must have a rather long tapering point with a fine opening and a rubber nipple that fits perfectly. The test is conducted by first expelling the air from the dropper by pinching the nipple. It is then filled with urine and again compressed to expel about half the contents. The outside is now wiped free from urine and the tip inserted into nitric acid, the nipple expanded and the

(1) Muenchen. med. Woch., Aug. 15, 1905.
(2) Muench. med. Woch., June 1, 1906.
(3) N. Y. Med. Jour., Aug. 25, 1906.

tube again filled. The urine and acid are now in sharp contact at about the middle of the tube. After standing point down for a few minutes the reaction may be noted. Should the result be in doubt it may be further proven that the ring is positive by slowly compressing the nipple when the ring will be seen to widen as it passes into the point of the dropper.

Tognetti[1] uses a tanno-hydrochloric test for albumin in urine. This reagent is sensitive to show albumin in proportion of 1:200,000 parts in urine. Bile interferes with the test and when present it must be removed by addition of two per cent. glacial acetic acid. The test described by the author is made with an equal amount of alcohol solution of tannin and urine. The mixture is heated somewhat and 33 per cent. hydrochloric acid, equal in amount to the urine present, is added. Opacity and a yellow white precipitate show presence of albumin.

Blood Test. Klinoff[2] recommends that urine be tested for blood by adding a quantity of hydrogen peroxid and then adding a small amount of aloin powder. Upon mixing thoroughly the urine turns purple. The urine should be freed from pus and should be acid. Albumin does not interfere with the reaction, but bile does. If the mixture is heated the reaction develops more rapidly.

Urea Determination. Meeker's apparatus[3] is shown in the accompanying illustration. It is made entirely of thin glass, about 8/10 mm. in thickness. A is a two-necked flask. The other parts of the apparatus are adapted to A by ground joints at B and C. D is a stop-cock with oblique bore, E. The tube F is graduated so that either $12\frac{1}{2}$ c.c. or 25 c.c. of urine may be measured from it into A. A stopper, carrying a capillary tube, H, is ground into F at G. The tube marked I, J, K, L has a capillary ending at I, and is ground into C at its lower end. L, K and J are, respectively, ferrous sulphate, soda-lime, and calcium chlorid. These are all in a granular state, capable of passing a sieve having twenty meshes to the linear inch, and of being retained on a sieve having eighty meshes to the linear inch. Each powder is retained

(1) Gazzetta degli Osped., No. 57.
(2) Russky Vrach, No. 16, 1906.
(3) Medicine, May, 1906.

in place by a suitable plug of absorbent cotton. M represents 50 c.c. of a freshly made solution of sodium hypobromite. This solution is made by the following formula:

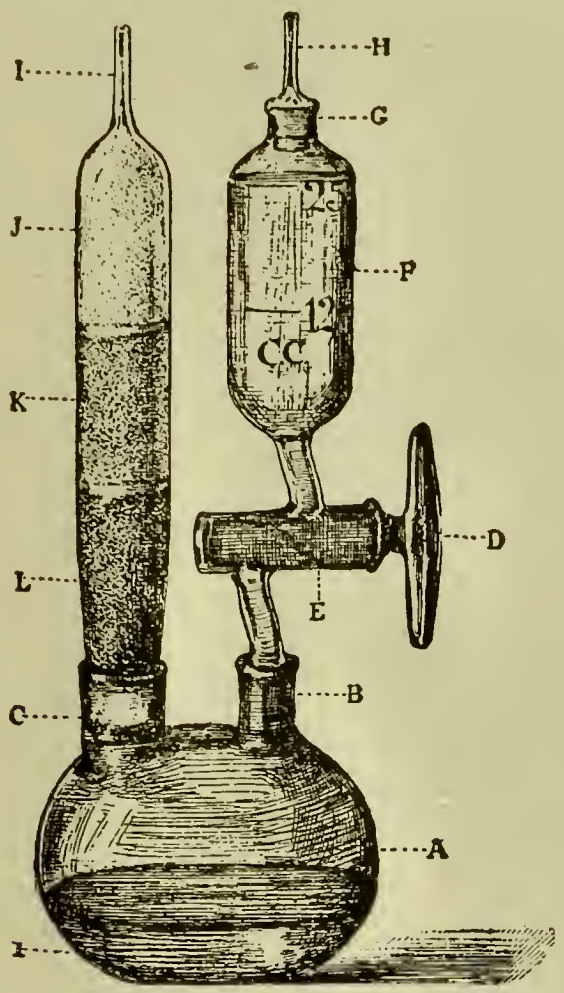

Fig. 12. Meeker's apparatus.

Sodium hydroxid	100 gm.
Water	250 c.c.
Allow to cool and then add slowly:	
Bromin	25 c.c.

A known weight of urine is introduced into F, the cock, D, being closed. The exterior of the apparatus is wiped dry, and the whole apparatus is then weighed. The apparatus is now removed from the balance, and the urine run into the sodium hypobromite solution. Nitrogen and other gases are evolved. Of these gases, nitrogen alone escapes, through the tube, I—the other gases being retained in the apparatus by the sodium hypobromite solution, or by the granular solids in the exit tube. The

apparatus is now set aside for thirty minutes, to permit the completion of the reactions and to cool. It is then weighed again. The difference between the two weights is the weight of nitrogen lost from the apparatus. Now calculate the percentage of urea in the urine.

Calculations are as follows:

Formula for urea, CON_2H_4.
Molecular weight of urea, 60.112.
Nitrogen in urea molecule, 28.08.
Let a = weight of urine used,
And b = weight of nitrogen lost from apparatus,
And P = percentage of urea in the urine,

$$\text{Then } P = \frac{\frac{60.112}{28.08}\,b}{a} \times 100 = 214.074\frac{b}{a}$$

Or, when great accuracy is not required, and 25 c.c. urine is employed, the urine used may be assumed to weigh 25 grammes, and the equation becomes

$$P = 8.563\ b.$$

Or, in urines rich in urea, when 12.5 c.c. of urine is employed, the percentage is obtained by the following equation:

$$P = 17.126\ b.$$

Methyl Blue Tests of Urine. Dunger[1] discusses the methyl blue test of urine that has been proposed by Russo as a supplemental or verifying test to the diazo-reaction. The test consists in the addition of four drops of a 1 per cent. solution of methylen blue to 4-5 c.c. of urine. A positive reaction is evidenced by the resulting marine-green color, while a blue green or blue is considered as negative. The reaction, according to Russo, is a valuable diagnostic aid in those conditions where the diazo-reaction would be used. The observations reported in the present article show that this reaction occurs in a greater number and variety of disease conditions than the diazo-reaction.

(1) Deutsche med. Woch., Sept. 27, 1906.

It was only at times that it occurred parallel to the diazo-reaction, and it therefore cannot be considered as a supplemental test. Its appearance does not allow of any diagnostic or prognostic conclusions. The reaction is not dependent upon a chemical reaction, but is due to a color mixture between the reagent and the urine and it is primarily dependent upon the tinctorial properties of the urine specimen. Clinically, the test is of no value.

Test for Bile Pigments. A. Raphiel[1] describes a method of testing for bile pigments in the urine which has been very satisfactory in his experience. He uses the well-known diazo reaction—first, sulfanilic acid (5.0), muriatic acid (50.0), distilled water (100.), and, second, sodium nitrate (.5) and distilled water (100.0). For the first test he puts 2 or 3 drops of the soda solution with about 5 c.c. of the other and adds 5 c.c. of the urine to be examined. The presence of bile pigments will show itself, first, in an amethyst color, passing in a short time to a cherry red. The intensity of the color increases in icterics during the first 24 hours. If the urine is very diluted, the red color is still visible against a white background. A second test is given as follows: To 2 or 3 drops of the soda solution added to the urine the sulfanilic acid is then added, and the fluid, according to the quantity of bile pigments present, takes on a more or less intense yellowish-green color, passing in the 24 hours to the above-described cherry red.

Sugar Test. Wagner[2] describes the "fermentation" sacharo-manometer shown in illustration (Fig. 13). It is used by filling the large bulb and arm to the mark 0 on the scale with mercury; the arm B is open above. Into the fermentation bottle, C, is placed 0.5 c.c. of the urine, and if not acid it is rendered so by the addition of a few drops of tartaric acid. Several drops of a fresh compressed yeast emulsion are added and the bottle attached in place. A small opening passes through the neck of the bottle and the tube for the purpose of adjusting the internal pressure. When this is correct the openings are pushed apart. Fermentation then proceeds. The mercury rises and the

(1) St. Petersburg. med. Wochenschr., No. 14.
(2) Muench. med. Woch., Nov. 28, 1905.

percentage of sugar under the temperature conditions may be read off the scale.

Sputum Sedimentation. Sachs[1] recommends the following procedure for the collection and preservation of sputum: The expectoration is collected in a bottle containing sufficient hydrogen peroxid to break up the mass

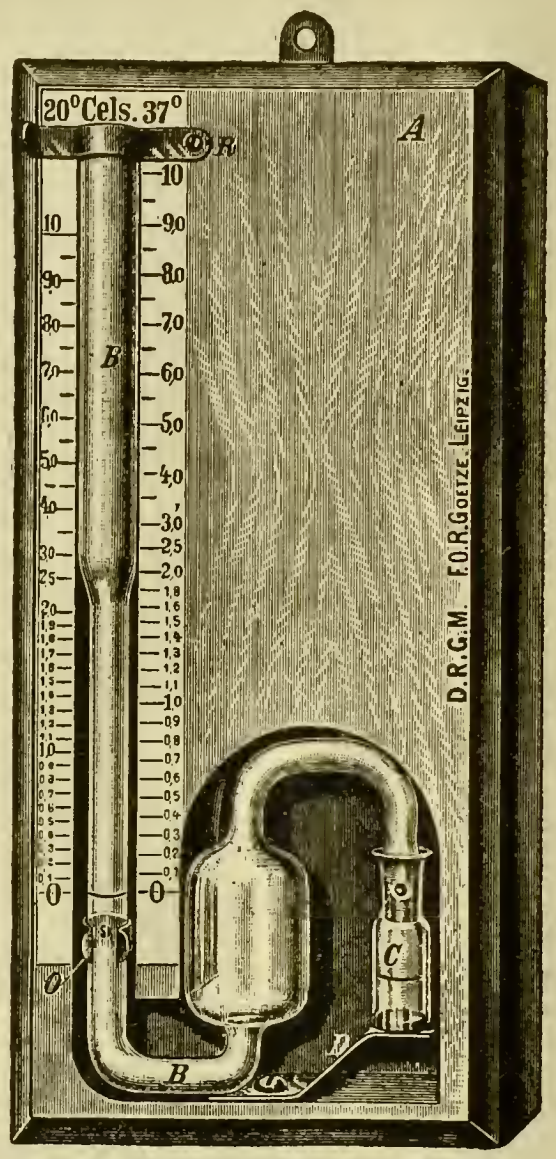

Fig. 13. Wagner fermentation sacharo-manometer.

and liberate the essential portions. The portion that settles at the bottom may be collected and further preserved by the addition of 1/1000 bichlorid of mercury solution. The staining properties of *B. tuberculosis* are not affected by the hydrogen peroxid.

Test for Semen. The Barberio reaction for spermatic

(1) Muenchen. med. Woch., Vol. LIII. No. 34, 1906.

fluid has been studied by Levinson,[1] who reports that the test is specific and that it is available in the absence of spermatozoa.

The test consists in the addition to the suspected material of a concentrated aqueous solution of picric acid, drop by drop, heating between each so as to cause concentration; if positive, yellowish rhombic crystals will be deposited. The crystals are not due to spermatozoa, but to some constituent of the prostatic or seminal secretion.

The medico-legal value of this test is very great, because, so far as known, this is the only test for semen outside of microscopic examination.

(1) Berlin. klin. Woch., Vol. XLIII, No. 41, 1906.

DICTIONARY
OF
NEW MEDICAL WORDS

BY
WILLIAM HEALY, A. B. (HARV.) M. D.

DICTIONARY OF NEW MEDICAL WORDS.

A

Abscess, Fixation a. An artificial abscess produced usually by injection of turpentine during the course of an acute infection for the theoretical purpose of attracting and fixing there the micro-organisms already in the body.

Acid, Tuberculinic a. A toxic acid isolated from the substance of tubercle bacilli.

Actinium. A rare radio-active metal not at present applicable to medical uses.

Addiment. The same as complement, q. v.

Adrenalitis. Inflammation of the suprarenal glands. When acute the symptoms are said to be pain in the lumbar region, vomiting, diarrhea and prostration.

Alcoholase. An enzyme contained in yeast.

Amaas. Kaffir milk-pox. A specific contagious eruptive fever somewhat resembling small-pox.

Amnesia of Broca. Pure word aphasia. Inability to remember spoken words.

Amnesiac. The person with lack of ability to remember.

Anemia, Porto Rican a. The extreme anemia due to uncinariasis, q. v.

Antimicrobin. The same as bacteriolysin, q. v.

Antirennene. A substance developed in blood serum following injection of rennet into the organism. It impedes the action of rennet on milk.

Aphasia, Ageusic a. [Gr. ageustos, not tasting.] Inability to remember words relating to the sense of taste.

Aphasia, Anosmic a. [Gr. osme, smell.] Inability to remember words related to the olfactory sense.

Aphasia, Commissural or conduction a. The mental condition in which words can be read or repeated correctly, but are not connected with the idea or thing they stand for.

Aphasis letheca. [Gr. lethe, forgetfulness.] Inability to remember the correct word. Aphasia amnesica.

Aphasia, Psychosensory a. Loss of power to comprehend language written, spoken or expressed in any way.

Aphasia, Wernicke's a. The same as commissural aphasia, q. v.

Aphasiac. The person with inability to speak from brain disease.

Aphesis. [Gr. to let go.] A mistake in speaking. A slip of the tongue.

Aphrasia. Inability or inaptitude for forming phrases.

Apoplexia uteri. Sudden hemorrhage from the uterus caused by arterial degeneration or hemorrhagic infarct.

Appendicitis larvata. A chronically recurring form of appendicitis as distinguished from a chronic residual appendicitis.

B

Bacteriotropic. The essential quality of a substance contained in serum which renders bacteria in that serum more liable to phagocytosis. Said to differ from opsonin by the fact that it is not destroyed by low degrees of heat.

Bundle of His. A muscular band, discovered by His, Jr., connecting the auricles with the ventricles. It runs posteriorly in the septum of the ventricles, passing into the musculature of the right auricle and its valves.

C

Cancrology. The sum of what is known concerning carcinoma.

D

Diastema. A term applied to the intertubular connective tissue of the testicle, which tissue is to be regarded as an interstitial gland.

Domicilium. A pneumatic chamber for treatment of a patient by either compressed or rarefied air.

Dressing, Tegmin d. White, aseptic, adhesive substance used as substitute for collodion. Said to be composed of emulsion of wax, acacia, water, zinc oxid and lanolin.

E

Endoaneurismorrhaphy. An operation for obliteration of the sac of an aneurism by opening it and ligating all of its internal orifices.

Endotheliolysin. The antibody which has the power of causing dissolution of endothelial tissue.

Entameba. Any ameba present as a parasite in the body. *E. dysenteriae* is a cause of tropical dysentery and is easily distinguished microscopically from *E. coli,* which is a very common parasite and probably innocuous.

Exohysteropexy. An operation for suspension or fixation of the uterus by means of extra-peritoneal implantation of the uterine fundus in the abdominal wall.

F

Fever, Chitral f. An acute infectious disease endemic in the Chitral Valley, India.

Formes frustes (form frust) [French]. Atypical form of any disease.

G

Gastroptyxy. An operation for reducing the size of a dilated stomach by passing a series of threads parallel through the outer coat of the stomach wall on to anterior aspect from upper to lower margin and then drawing them tight.

Goundou. A disease of tropical Africa, characterized by bilateral tumors at the base of the nose. The growths are hard, insensitive and probably a hyperplasia due to inflammation.

H

Haptophile. That part of the cell ceptor which has peculiar affinity a haptophore.

Heart-block. Interruption of tra mission of impulses from auricles ventricles, which may result in crease of intersystolic pause or independent contractions of auri and ventricles. It may ca Stokes-Adams' syndrome. Etiol in some cases at least is disease the bundle of His, q. v.

Hemorrhagin. The lysin which present in snake venom and has power of destroying endothelial sue and so causing the charact istic hemorrhagic extravasations lowing snake bite.

Hepaptosia. Wandering or descen liver.

Hydradenoma. A neoplasm origin ing in mal-developed sweat gland

Hyperpyremia. [Gr. pyr, fire, t which burns.] A humoral condit implying a pathological accumulat in the blood of unoxidized carbo aceous material derived from blood supply.

I

Insufficiency, Diastemic i. A lack internal secretion in the testicles, distinguished from absence of spermatazoa. The result of a pa ologic diastema, q. v. This insu ciency causes various bodily abn malities at puberty and later.

Itch, Ground i. The same as ma morria, q. v.

L

Lac-bismo. A proprietary combi tion of bismuth hydroxid and s carbonate suspended in liquid c taining 2½ grains to the dram.

Lethologica. [Gr. lethe, forgetf ness.] Inability to remember correct word. Aphasia amnesica.

Lipase. A fat-splitting enzyme fou in the pancreatic juice, in bl plasma and in several plants. T same as steapsin.

M

Mazamorria. The "ground itch" wh is the first sign of entrance into skin of the feet by the *Uncinaria vae.*

Metrorrhagia myopathica. Uterin hemorrhage in women who have borne children, resulting from insufficient contractile power of the uterin musculature.

Microdentism. The condition of having smaller teeth than normal.

Microspironema. A name offered for the recently discovered germ of syphilis. Vide Treponema.

N

Nephroson. A proprietary diuretic sourwood compound.

O

Organotherapy, Heterologous o. Treatment by substances of animal origin having no relationship to the special organs diseased in the patient.

Organotherapy, Homologous o. Treatment by which deficiency in the function of a certain organ is relieved by administration of remedial derivative from similar organs of the lower animals.

P

Pallanesthesia. Inability to perceive the kind of sensation produced by the tuning-fork applied to some portion of the body. Coincides with loss of the muscular sense.

Pallesthesia. The sensation experienced upon the application of the tuning-fork to some portion of the body. A function of the fine nerve fibers of all the subcutaneous tissues and not of cutaneous sensibility.

Paludides. [L. palus, swamp.] Any cutaneous eruptions resulting from malarial infection.

Pegnin. A powder to be added to cow's milk to aid its digestion by infants. The milk is first coagulated and then the curds are finely divided by shaking.

Peptid. A proteid body artificially produced by blending various amino-acids. A series of peptids have been produced and they all present the important characteristic reactions of the peptones.

Perialienitis. Inflammation in the neighborhood of a foreign body, particularly in the neighborhood of a biliary concretion.

Phrenoptosis. Downward displacement of the diaphragm.

Polynucleosis. The condition of having many polynuclear cells in the blood or in an exudate.

Polypeptid. Crystalline, soluble chemical bodies giving the biuret reaction and split up by trypsin. They are artificially produced by uniting some of the elementary components of proteid molecules which have been disintegrated by hydrolysis.

Pyremia. [Gr. pyr. fire, that which burns.] The condition of the blood which contains carbonaceous matter not in excess of the physiological capacity of the organism.

Q

Quadriplegia. Paralysis of all four limbs.

R

Radioactivity. The property possessed by a substance of expelling from itself charged particles of matter capable of passing through the interspaces of other matter and so producing kinetic, thermal, electric or chemical phenomena.

Radiode. Metallic capsules containing radium with aluminum or mica windows and attached to various holders for treating the interior of the body.

Radiogram. A shadow picture or photograph made by radium.

Radiologist. A person who is versed in the theory and use of the various emanations from radioactive substances.

Radion. One of the actual material particles thrown off by radioactive substances and which go to form certain parts of their rays. Radions are also called emanations and corpuscles.

Rays, Alpha r. Those emanations from radioactive substances which have the lowest velocity and the lowest penetration. They are electrically positive.

Rays, Becquerel r. Those emanations or radiations which constantly and spontaneously are given forth by uranium, radium and other radioactive substances.

Rays, Beta r. Those emanations from radioactive substances which have

medium velocity and penetration and are electrically negative. Analgous to cathode rays.

Rays, Crookes' r. The same as cathode rays.

Rays, Gamma r. Those emanations from radioactive substances which do not behave like projectiles, have enormous velocity, and great penetration. Analgous to Roentgen rays.

Reaction, Desmoid r. [Gr. desmos, a ligament.] A test for stomach secretion and motility. Methylen blue and iodoform are tied in rubber tissue with a string of soft catgut which is always digested by normal gastric juice and the stain liberated if the little bag remains the normal length of time in the stomach. The stain appears in the urine normally after five or six hours.

Rhodan. A salt of sulfocyanic acid which occurs in the nasal secretion.

Rodagen. A preparation made from the milk of goats deprived of their thyroid glands. Suggested for treatment of exophthalmic goiter. Dose, 1 to 2½ drams a day.

S

Sanoform. Methyl ether of diiodosalicylic acid. White, odorless powder soluble in alcohol, ether and vaselin. Used as surgical dressing in powder or ointment.

Seismethesia. [Gr. seismos, a shaking.] Perceptions of vibrations produced in a liquid or aerial medium. Due to the tactile sense.

Septoform or Septoforma. A condensation product of formaldehyd dissolved in alcoholic solution of linseed oil potassium soap. An antiseptic and disinfectant used in 3 to 10 per cent. solution in veterinary practice.

Serum, Anti-tetanic s. Serum derived from immunized animals which can prevent or overcome the action of tetanus toxin. The serum is sometimes dried and used as a prophylactic powder applied to the wound.

Serum, Lymphatotoxic s. A serum which destroys lymphocytes.

Serum, Pane's. Taken from turkeys and used in the treatment of pneumonia.

Sevetol. Emulsion of mixed predigested animal and vegtable fats. Dose, ¼ to 1 ounce in milk, wat or wine.

Sign Vanzetti's s. (For different diagnosis of various scolioses.) T pelvis in sciatica is always horizo tal in spite of marked scoliosis. other lesions with scoliosis, such hip-joint disease, the pelvis is mo or less inclined.

Simesthesia. Osseous sensibility. T perception of vibrations, as of tuning-fork, directly applied to t bone. This sense may be preserv when tactile sensation is lost.

Sodium aurate. An antiseptic whi in half per cent. solution is said be non-irritating to tissue cells a strongly germicidal.

Stagnin. A preparation derived fro spleen pulp of horses by antisept autolysis. Produces by chemical a tion prompt coagulation of bloo Dose by intramuscular injection, to 60 minims a day.

Striae cutis distensae. The perma nent appearances left in the sk after abnormal distention. Resul from tears in the cutis layers. T principal type is the *Linea albicant* found after pregnancy and aft ascitic distention.

Styracol. Guaiacol cinnamic este White powder insoluble in wate Given in phthisis and for intestin disinfection. Dose, 15 to 120 grai per diem.

Succinimid, Mercuric s. A salt mercury used in 5 per cent. with per cent. cocain for hypodermic i jection in treating syphilis.

Sulfosot. Potassium creosote sulfo ate. Used in treatment of tuberc losis. Dose, 5 to 20 grains.

T

Tanformal. A proprietary intestin astringent and disinfectant.

Test, Sahli's desmoid t. Vide Rea tion, Desmoid r.

Tetanospasmin. A toxic substan produced by the tetanus bacill which causes the spasms of tetanu

Thermit. A powdery mixture of al minum and either ferric or ferro oxid. Used with a reagent to pr duce intense heat for a few secon in order to rapidly sterilize wat for drinking purposes.

Thoriagram. A shadow picture or photograph made by thorium.

Thorium. A rare metal, recently found more abundantly and used extensively in production of incandescent mantles for lighting. It is mildly radioactive and may be used directly as thorium oxid or in 25 per cent. ointment. Thorium emanations may be inhaled for tuberculosis.

Thorium X. A substance resulting in chemical action of thorium atoms and which directly produces its radioactivity. The most powerful rays are obtained from hot thorium oxid.

Thrombokinase. A fibrin-forming substance of the blood.

Tonaphasia. Inability to remember a lately familiar tune, while musical notes may be understood.

Toxolysin. The same as antitoxin, q. v.

Toxophile. That part of the cell receptor which has peculiar affinity for a toxaphore.

Treponema pallidum. The more recent name for the organism of syphilis, previously called a spirochæte, but later discovered to be a new species.

Treponemiasis. A name properly given to syphilis if the organism of that disease is Schaudinn's treponema.

Typhase. Bacteriolytic enzyme of the typhoid bacillus.

U

Ureine. A compound isolated from urine. Perhaps the result of treating it with chemicals.

Uremides. Skin eruptions, essentially erythematous, resulting from the symptom complex of toxic absorption often called uremic poisoning.

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